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TO: Dwayne C Jones Location: 3b87 / 3c70 Wednesday, May 10, 2006 Art Unit: 1614 Phone: 571-272-0578 Serial Number: 10 / 528114	From: Jan Delaval Location: Biotech-Chem Library Remsen 1a51 Phone: 571-272-2504 jan.delaval@uspto.gov

Search Notes

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SEARCH REQUEST FORM

Requester's Full Name: Dwayne C. Jones Examiner #: 71299 Date: 16 APR 06

Art Unit: 1614 Phone Number: 2-0578 Serial Number: 10/529,114

Location (Bldg/Room#): 3B87 (Mailbox #): 3C70 Results Format Preferred (circle): PAPER DISK

RGM

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: see attached cover sheet MG

Inventors (please provide full names):

Earliest Priority Date: 16 SEP 2002

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search claims 1, 4, 5-7

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Searcher: [signature]

Searcher Phone #: 22504

Searcher Location:

Date Searcher Picked Up: 5/10/06

Date Completed: 5/10/06

Searcher Prep & Review Time: 30

Online Time: 60

Type of Search

___ NA Sequence (#)

___ AA Sequence (#)

✓ Structure (#)

✓ Bibliographic

___ Litigation

___ Fulltext

___ Other

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✓ STN ___ Dialog

___ Questel/Orbit ___ Lexis/Nexis

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___ Commercial ___ Oligomer ___ Score/Length

___ Interference ___ SPDI ___ Encode/Transl

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Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact:***

Mary Hale, Information Branch Supervisor
22507, Remsen 1d86

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk

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STRUCTURE FILE UPDATES:    9 MAY 2006  HIGHEST RN 883631-57-0
DICTIONARY FILE UPDATES:   9 MAY 2006  HIGHEST RN 883631-57-0

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*                                                                    *
* The CA roles and document type information have been removed from *
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*                                                                    *
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=> d sta que 149
L47             STR
N @22    O @23


     18
     O
     :
     :
     :
G2---C-G1-C=C-CH2-C=C-CH2-C=C-CH2-C=C-CH2-C=C-Et
17  15 13  7  5  3    1  2  4    6  8  10   12  14 16   19 20 21

REP G1=(3-3) CH2
VAR G2=22/23
NODE ATTRIBUTES:
CONNECT IS M1  RC AT  22
CONNECT IS M1  RC AT  23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L49          756 SEA FILE=REGISTRY CSS FUL L47

100.0% PROCESSED   17708 ITERATIONS                          756 ANSWERS
SEARCH TIME: 00.00.01


=> d his

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               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 10:51:37 ON 10 MAY 2006
                 E HORROBIN/AU
L1           586 S E5,E8,E12-E16
                 E AYTON/AU
L2             2 S E4
                 E CLARKSON S/AU
L3            29 S E3-E6,E13
L4          8204 S EICOSAPENTAENOIC ACID OR EICOSAPENTAENOATE

     FILE 'REGISTRY' ENTERED AT 10:53:31 ON 10 MAY 2006
L5             1 S 10417-94-4
                 E C20H30O2/MF
L6            17 S E3 AND 5 8 11 14 17
L7             8 S L6 AND EICOSAPENTAENOIC ACID
L8             6 S L7 NOT LABELED
                 SEL RN
L9           160 S E1-E6/CRN
L10            6 S L5,L8

     FILE 'HCAPLUS' ENTERED AT 10:56:25 ON 10 MAY 2006
L11         9679 S L10
L12          652 S ICOSAPENT OR ICOSAPENTAENOIC ACID OR ICOSAPENTAENOATE OR TIMN
L13        12866 S L4,L11,L12
L14          100 S L9
L15          145 S L1-L3 AND L13
L16           12 S L1-L3 AND L14
L17          146 S L15,L16
                 E ANOREXIA/CT
                 E E3+ALL
L18         2355 S E2,E3
L19         7622 S ANOREX? OR ANOREX?(S)NERVOSA?
                 E BULIMIA/CT
                 E E3_ALL
                 E BULIMIA/CT
                 E E3+ALL
L20          932 S E1,E2
L21         1171 S BULIMI?
                 E EATING DISORDER/CT
                 E E4+ALL
L22         1983 S E2
L23         1432 S E1
L24            4 S L1-L3 AND L18-L23
L25            1 S L24 AND L17
L26            3 S L24 NOT L25
L27            1 S L26 AND 141:105641/DN
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L28           2 S L25,L27
L29          54 S L17 AND P/DT
                E BODY WEIGHT/CT
L30       22053 S E3-E5
                E E3+ALL
L31       64675 S E2 OR E5+OLD,NT OR E6+OLD,NT OR E7+OLD,NT OR E8+OLD,NT
L32         475 S L13 AND L30,L31
L33          22 S L32 AND L18-L23

     FILE 'REGISTRY' ENTERED AT 11:04:16 ON 10 MAY 2006
L34           1 S 25378-27-2
L35          17 S 25378-27-2/CRN

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L36        1055 S L34 OR L35
L37           2 S L36 AND L18-L23
L38          30 S L36 AND L30,L31
L39           2 S L37 AND L38
L40          22 S L33,L39
L41          11 S L1-L3 AND L36
L42           0 S L41 AND L39
L43           0 S L41 AND L40
                SEL AN L40 4 7-9 12 16-21
L44          11 S L40 AND E1-E22
L45          13 S L28,L44
L46          13 S L45 AND L1-L4,L11-L33,L36-L45

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L48          36 S L47 CSS
L49         756 S L47 CSS FUL
                SAV L49 JONES528/A
L50         590 S L49 NOT L9,L10

     FILE 'HCAPLUS' ENTERED AT 11:21:15 ON 10 MAY 2006
L51         712 S L50
L52           1 S L51 AND L18-L23
L53           7 S L51 AND L30,L31
L54           8 S L52,L53
L55           0 S L46 AND L51

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FILE LAST UPDATED: 9 May 2006 (20060509/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l46 all hitstr tot

L46 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2005:136529** HCAPLUS
DN 142:212406
ED Entered STN: 17 Feb 2005
TI Method for treating cachexia with RXR retinoid ligands
IN Jiang, Guang Liang; Yuan, Yang-Dar; Chandraratna, Roshantha A.
PA Allergan, Inc., USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K0031-00
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005013949	A2	20050217	WO 2004-US25564	20040806
	WO 2005013949	A3	20050915		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004263156	A1	20050217	AU 2004-263156	20040806
	CA 2535260	AA	20050217	CA 2004-2535260	20040806
PRAI	US 2003-493138P	P	20030807		
	US 2003-533734P	P	20031231		
	WO 2004-US25564	W	20040806		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2005013949	ICM	A61K0031-00
	IPCI	A61K0031-00 [ICM,7]
	IPCR	A61K0031-185 [I,C]; A61K0031-192 [I,A]; A61K0031-196 [I,A]; A61K0031-341 [I,A]; A61K0031-341 [I,C]; A61K0031-343 [I,A]; A61K0031-343 [I,C]; A61K0031-381 [I,A]; A61K0031-381 [I,C]; A61K0031-385 [I,A]; A61K0031-385 [I,C]; A61K0031-44 [I,A]; A61K0031-44 [I,C]; A61K0031-505 [I,A]; A61K0031-505 [I,C]
	ECLA	A61K031/192; A61K031/196; A61K031/341; A61K031/343; A61K031/381; A61K031/385; A61K031/44; A61K031/505
AU 2004263156	IPCI	A61K0031-185 [I,C]; A61K0031-341 [I,C]; A61K0031-343 [I,C]; A61K0031-381 [I,C]; A61K0031-385 [I,C]; A61K0031-44 [I,C]; A61K0031-505 [I,C]; A61P0003-00

[I,C]; A61P0025-00 [I,C]; A61P0035-00 [I,C]; A61K0031-192 [I,A]; A61K0031-196 [I,A]; A61K0031-341 [I,A]; A61K0031-343 [I,A]; A61K0031-381 [I,A]; A61K0031-385 [I,A]; A61K0031-44 [I,A]; A61K0031-505 [I,A]; A61P0003-00 [I,A]; A61P0025-00 [I,A]; A61P0035-00 [I,A]

CA 2535260 IPCI A61K0031-192 [I,A]; A61K0031-196 [I,A]; A61K0031-341 [I,A]; A61K0031-343 [I,A]; A61K0031-381 [I,A]; A61K0031-385 [I,A]; A61K0031-44 [I,A]; A61K0031-505 [I,A]; A61P0003-00 [I,A]; A61P0025-00 [I,A]; A61P0035-00 [I,A]

OS MARPAT 142:212406

AB The invention discloses a method for the treatment of cachexia in a subject in need of treatment. More specifically, the invention discloses the use of retinoid compds. that act on retinoid X receptors (RXRs) for the treatment of cachexia in a subject in need of treatment. The cachexia is associated with a complication of a primary disease, condition or disorder. Primary diseases, conditions and disorders include, but are not limited to, cancer, AIDS, liver cirrhosis, diabetes mellitus, chronic renal failure, chronic obstructive pulmonary disease, chronic cardiac failure, immune system diseases (e.g., rheumatoid arthritis and systemic lupus erythematosus), tuberculosis, cystic fibrosis, gastrointestinal disorders (e.g., irritable bowel syndrome and inflammatory bowel disease), Parkinson's disease, **anorexia nervosa**, dementia, major depression, an aged condition, and sarcopenia.

ST cachexia treatment RXR retinoid ligand

IT Appetite
Body weight
Cachexia
Combination chemotherapy
Hypolipemic agents
(RXR retinoid ligands for cachexia treatment)

IT Hyperlipidemia
Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RXR retinoid ligands for cachexia treatment)

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RXRΓ; RXR retinoid ligands for cachexia treatment)

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RXRα; RXR retinoid ligands for cachexia treatment)

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RXRβ; RXR retinoid ligands for cachexia treatment)

IT Thyroid hormones
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and analogs; RXR retinoid ligands for cachexia treatment)

IT Appetite
(**anorexia nervosa**, cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Sequestering agents
(bile acid sequestrants; RXR retinoid ligands for cachexia treatment)

IT AIDS (disease)
Aging, animal
Biliary tract, neoplasm
Cirrhosis
Cystic fibrosis
Diabetes mellitus

Digestive tract, disease
Digestive tract, neoplasm
Esophagus, neoplasm
Immune disease
Leukemia
Liver, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Neoplasm
Pancreas, neoplasm
Parkinson's disease
Tuberculosis
(cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Biological transport
(cholesterol absorption inhibitors; RXR retinoid ligands for cachexia treatment)

IT Lung, disease
(chronic obstructive pulmonary disease, cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Intestine, neoplasm
(colorectal, cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Mental and behavioral disorders
(dementia, cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Heart, disease
Kidney, disease
(failure, chronic, cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Mental and behavioral disorders
(major depression, cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Lung, neoplasm
(non-small-cell carcinoma; RXR retinoid ligands for cachexia treatment)

IT Drug delivery systems
(oral; RXR retinoid ligands for cachexia treatment)

IT Carcinoma
(pulmonary non-small-cell; RXR retinoid ligands for cachexia treatment)

IT Carcinoma
(pulmonary small-cell; RXR retinoid ligands for cachexia treatment)

IT Muscle
(sarcopenia, cachexia associated with; RXR retinoid ligands for cachexia treatment)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequestrants; RXR retinoid ligands for cachexia treatment)

IT Lung, neoplasm
(small-cell carcinoma; RXR retinoid ligands for cachexia treatment)

IT Muscle, disease
(wasting; RXR retinoid ligands for cachexia treatment)

IT 59-67-6, Nicotinic acid, biological studies 59-67-6D, Nicotinic acid, derivs. 70-26-8, Ornithine 78-41-1, Triparanol 83-46-5, β-Sitosterol 90-26-6, α-Phenylbutyramide 313-05-3, Azacosterol 503-49-1, Meglutol 541-15-1, Carnitine 597-71-7, Pentaerythritol Tetraacetate 943-45-3D, Fibric acid, derivs. 959-10-4, Xenbucin 1239-29-8, Furazabol **1553-41-9**, 5,8,11,14,17-**Eicosapentaenoic acid** 4091-75-2, Clomestrone 5108-94-1, Mytatrienediol 6964-20-1, Tiadenol 7236-47-7 9007-28-7, Chondroitin Sulfate 9011-18-1, Dextran Sulfate Sodium 9064-91-9, Detaxtran 11042-64-1, γ-Oryzanol 14417-88-0, Melinamide

16816-67-4, Pantethine 23288-49-5, Probucol 23602-78-0, Benfluorex 23918-98-1, Eritadenine 54110-25-7, Pirozadil 57775-26-5, Sultosilic Acid 72420-38-3, Acifran 153559-49-0 186134-48-5 474654-29-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RXR retinoid ligands for cachexia treatment)

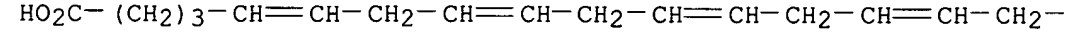
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(absorption inhibitors; RXR retinoid ligands for cachexia treatment)

IT 9028-35-7, HMG-CoA reductase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; RXR retinoid ligands for cachexia treatment)

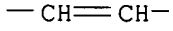
IT **1553-41-9**, 5,8,11,14,17-**Eicosapentaenoic acid**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RXR retinoid ligands for cachexia treatment)

RN 1553-41-9 HCAPLUS
CN 5,8,11,14,17-Eicosapentaenoic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L46 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2004:941903** HCAPLUS
DN 142:481325
ED Entered STN: 08 Nov 2004
TI Effect of fish oil on appetite and other symptoms in patients with advanced cancer and **anorexia**/cachexia: a double-blind, placebo, controlled study
AU Bruera, Eduardo; Strasser, Florian; Palmer, J. Lynn; Willey, Jie; Calder, Kathryn; Amyotte, Gail; Baracos, Vickie
CS Department of Palliative Care and Rehabilitation Medicine, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SO Journal of Clinical Oncology (2003), 21(1), 129-134
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal
LA English
CC 18-5 (Animal Nutrition)
Section cross-reference(s): 1
AB The aim was to determine whether high doses of fish oil, administered over 2 wk, improve symptoms in patients with advanced cancer and decreased weight and appetite. Sixty patients were randomly assigned to fish oil capsules or placebo. Appetite, tiredness, nausea, well-being, caloric intake, nutritional status, and function were prospectively assessed at days 1 and 14. The baseline weight loss was 16±11 and 16 8 kg in the fish oil (n = 30) and placebo (n = 30) group resp., whereas the baseline appetite (0 mm = best and 10 mm = worst) was 58±24 mm and 67±19 mm, resp. (P = not significant). The mean daily dose was 10±4 (fish oil group) and 9±3 (placebo group) capsules, which provided 1.8 g of **eicosapentaenoic**

acid and 1.2 g of docosahexaenoic acid in the fish oil group. No significant differences in symptomatic or nutritional parameters were found (P <.05), and there was no correlation between changes in different variables between days 1 and 14 and the fish oil doses. Finally, the majority of the patients were not able to swallow more than 10 fish oil capsules per day, mainly because of burping and aftertaste. Fish oil did not significantly influence appetite, tiredness, nausea, well-being, caloric intake, nutritional status, or function after 2 wk compared with placebo in patients with advanced cancer and loss of both weight and appetite.

ST fish oil appetite cancer **anorexia** cachexia
eicosapentaenoate docosahexaenoate

IT Drugs
(appetite stimulants; effect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

IT **Cachexia**
(cancerous; effect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

IT **Anorexia**
Appetite
Body weight
Fatigue, biological
Human
Neoplasm
Nutrition, animal
(effect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

IT Fats and Glyceridic oils, biological studies
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fish; effect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

IT Appetite
(stimulants; effect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

IT 24880-45-3
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bon s,ste b v,releffect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

IT 57-10-3, Hexadecanoic acid, biological studies 57-11-4, Octadecanoic acid, biological studies 60-33-3, 9,12-Octadecadienoic acid (9Z,12Z)-, biological studies 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 112-85-6, Docosanoic acid 373-49-9 506-17-2 506-30-9, Eicosanoic acid 506-32-1 544-63-8, Tetradecanoic acid, biological studies 5598-38-9 6217-54-5, DHA **10417-94-4** 17046-59-2 20290-75-9 28874-58-0 28929-01-3 28933-89-3 31152-46-2
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

IT 463-40-1
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seffect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Barber, M; Br J Cancer 1999, V81, P80 HCAPLUS
(2) Barber, M; Lipids 2001, V36, P347 HCAPLUS

(3) Beck, S; Cancer Res 1991, V51, P6089 HCAPLUS
(4) Bruera, E; Ann Oncol 1999, V10, P857 MEDLINE
(5) Bruera, E; Cancer 1990, V66, P1279 MEDLINE
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(8) Bruera, E; Cancer Treat Rep 1985, V69, P751 MEDLINE
(9) Bruera, E; Cancer Treat Rep 1986, V70, P981 MEDLINE
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(11) Bruera, E; Support Care Cancer 2001, V9, P162 MEDLINE
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(13) Dunlop, R; Cachexia-Anorexia in Cancer Patients 1996, P76
(14) Endres, S; N Engl J Med 1989, V320, P265 HCAPLUS
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(19) Kaasa, T; Palliat Med 2000, V14, P509 MEDLINE
(20) Maltoni, M; Ann Oncol 2001, V12, P289 MEDLINE
(21) Meydani, S; J Clin Investig 1993, V92, P105 HCAPLUS
(22) Nilsson, M; J Intern Med 2001, V250, P225 MEDLINE
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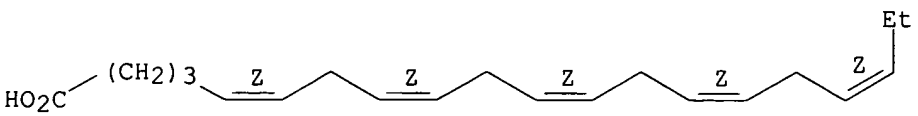
IT **10417-94-4**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of fish oil on appetite and other symptoms in cancer patients with **anorexia**/cachexia)

RN 10417-94-4 HCAPLUS

CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L46 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

AN **2004:941700** HCAPLUS

DN 142:260641

ED Entered STN: 08 Nov 2004

TI An **eicosapentaenoic acid** supplement versus megestrol acetate versus both for patients with cancer-associated wasting: a north central cancer treatment group and National Cancer Institute of Canada collaborative effort

AU Jatoi, Aminah; Rowland, Kendrith; Loprinzi, Charles L.; Sloan, Jeff A.;

Dakhil, Shaker R.; MacDonald, Neil; Gagnon, Bruno; Novotny, Paul J.; Mailliard, James A.; Bushey, Teresita I. L.; Nair, Suresh; Christensen, Brad
CS Mayo Clinic and Foundation, Rochester, USA
SO Journal of Clinical Oncology (2004), 22(12), 2469-2476
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal
LA English
CC 18-5 (Animal Nutrition)
AB Purpose Studies suggest **eicosapentaenoic acid** (EPA), an omega-3 fatty acid, augments weight, appetite, and survival in cancer-associated wasting. This study determined whether an EPA supplement-administered alone or with megestrol acetate (MA) - was more effective than MA. Patients and Methods Four hundred twenty-one assessable patients with cancer-associated wasting were randomly assigned to an EPA supplement 1.09 g administered bid plus placebo, MA liquid suspension 600 mg/d plus an isocaloric, isonitrogenous supplement administered twice a day; or both. Eligible patients reported a 5-lb, 2-mo weight loss and/or intake of less than 20 cal/kg/d. Results A smaller percentage taking the EPA supplement gained ≥ 10% of baseline weight compared with those taking MA: 6% v 18%, resp. (P =.004). Combination therapy resulted in weight gain of ≥ 10% in 11% of patients (P =.17 across all arms). The percentage of patients with appetite improvement (North Central Cancer Treatment Group Questionnaire) was not statistically different: 63%, 69%, and 66%, in EPA-, MA-, and combination-treated arms, resp. (P =.69). In contrast, 4-wk Functional Assessment of **Anorexia**/Cachexia Therapy scores suggested MA-containing arms experienced superior appetite stimulation compared with the EPA arm, with scores of 40, 55, and 55 in EPA-, MA-, and combination-treated arms, resp. (P =.004). Survival was not significantly different among arms. Global quality of life was not significantly different among groups. With the exception of increased impotence in MA-treated patients, toxicity was comparable. Conclusion This EPA supplement, either alone or in combination with MA, does not improve weight or appetite better than MA alone.
ST **eicosapentaenoate** supplement megestrol acetate cancer wasting
IT **Anorexia**
Appetite
Body weight
Cachexia
Human
Neoplasm
(**eicosapentaenoic acid** supplement vs. megestrol acetate vs. both for patients with cancer-associated wasting)
IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., omega-3; **eicosapentaenoic acid** supplement vs. megestrol acetate vs. both for patients with cancer-associated wasting)
IT 595-33-5, Megestrol acetate **25378-27-2, Eicosapentaenoic acid**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**eicosapentaenoic acid** supplement vs. megestrol acetate vs. both for patients with cancer-associated wasting)
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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IT **25378-27-2, Eicosapentaenoic acid**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**eicosapentaenoic acid** supplement vs. megestrol acetate vs. both for patients with cancer-associated wasting)

RN 25378-27-2 HCAPLUS
CN Eicosapentaenoic acid (8CI, 9CI) (CA INDEX NAME)

CM 1

CRN 506-30-9
CMF C20 H40 O2

$HO_2C-(CH_2)_{18}-Me$

L46 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2004:811404** HCAPLUS
DN 142:456951
ED Entered STN: 06 Oct 2004
TI Cancer-Related **Anorexia**/Cachexia Syndrome and Oxidative Stress: An Innovative Approach beyond Current Treatment
AU Mantovani, Giovanni; Madeddu, Clelia; Maccio, Antonio; Gramignano, Giulia; Lusso, Maria Rita; Massa, Elena; Astara, Giorgio; Serpe, Roberto
CS Department of Medical Oncology, University of Cagliari, Cagliari, Italy
SO Cancer Epidemiology, Biomarkers & Prevention (2004), 13(10), 1651-1659
CODEN: CEBPE4; ISSN: 1055-9965
PB American Association for Cancer Research
DT Journal
LA English
CC 1-12 (Pharmacology)
AB Objective: Cancer-related **anorexia**/cachexia syndrome and oxidative stress play a key role in the progression and outcome of neoplastic disease. Patients and Methods: On the basis of our previously

published studies and clin. experience, we have developed an innovative approach consisting of diet with high polyphenol content (400 mg), p.o. pharmaconutritional support enriched with n - 3 fatty acids (**eicosapentaenoic acid** and docosahexaenoic acid) 2 cans (237 mL each) per day, medroxyprogesterone acetate 500 mg/d, antioxidant treatment with α-lipoic acid 300 mg/d plus carbocysteine lysine salt 2.7 g/d plus vitamin E 400 mg/d plus vitamin A 30,000 IU/d plus vitamin C 500 mg/d, and selective cyclooxygenase-2 inhibitor Celecoxib 200 mg/d. The treatment is administered for 16 wk. The following variables are evaluated: (a) clin. variables (stage and Eastern Cooperative Oncol. Group performance status); (b) nutritional variables (lean body mass, appetite, and resting energy expenditure); (c) laboratory variables (serum levels of proinflammatory cytokines, C-reactive protein, and leptin and blood levels of reactive oxygen species and antioxidant enzymes); and (d) quality of life variables (European Organization for Research and Treatment of Cancer QLQ-C30, EQ-5Dindex, and EQ-5DVAS). A phase II nonrandomized study has been designed to enroll 40 patients with advanced cancer at different sites with symptoms of cancer-related **anorexia**/cachexia syndrome and oxidative stress. Results: As of Jan. 2004, 28 patients have been enrolled: 25 patients were evaluable and 14 of them have completed the treatment (20 patients have completed 2 mo of treatment). As for clin. response, five patients improved, three patients remained unchanged, and six patients worsened. The Eastern Cooperative Oncol. Group performance status (grade) 1 remained unchanged. As for nutritional/functional variables, the lean body mass increased significantly at 2 and 4 mo. As for laboratory variables, reactive oxygen species decreased significantly and proinflammatory cytokines interleukin-6 and tumor necrosis factor-α decreased significantly. As for quality of life, it comprehensively improved after treatment. Conclusions: The treatment has been shown to be effective for clin. response, increase of lean body mass, decrease of reactive oxygen species and proinflammatory cytokines, and improvement of quality of life. The treatment has been shown to be safe with good compliance of patients. The study is in progress (14 further patients will be included).

ST cancer **anorexia** cachexia syndrome oxidative stress antioxidant; celecoxib fatty lipoic acid carbocysteine lysine polyphenol medroxiprogesterone

IT Antioxidants
(antioxidant therapy with α-lipoic acid + carbocysteine lysine salt + vitamins E + A + C was well tolerated, effective, raised LBM, reduced ROS, proinflammatory cytokines and improved life quality in advanced cancer patient with CACS/OS)

IT Neoplasm
(polyphenol diet, n-3 fatty acids, progestagen, cyclooxygenase-2 inhibitor celecoxib and antioxidant therapy was well tolerated, effective for clin. response, raised LBM, reduced ROS, IL-6, TNF- in advanced cancer patient with CACS/OS)

IT **Anorexia**
Cachexia
Human
Oxidative stress, biological
(polyphenol diet, n-3 fatty acids, progestagen, cyclooxygenase-2 inhibitor celecoxib and antioxidant therapy was well tolerated, effective for clin. response, raised LBM, reduced ROS, IL-6, TNF-α in advanced cancer patient with CACS/OS)

IT Phenols, biological studies
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(polyphenols, nonpolymeric; diet with high polyphenol content was well tolerated, effective for clin. response and significantly increased

LBM, appetite, decreased ROS, proinflammatory cytokines and improved quality of life in advanced cancer patient with CACS/OS)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., omega-3; pharmaconutritional enriched with n-3 fatty acids (eicosapentaenoic, docosahexaenoic acid) was well tolerated, effective for clin. response and raised LBM, decreased ROS, proinflammatory cytokines in advanced cancer patient with CACS/OS)

IT Progestogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestagen medroxiprogesterone acetate was well tolerated, effective for clin. response and significantly raised LBM, appetite, reduced ROS, proinflammatory cytokines and improved quality of life in advanced cancer patient with CACS/OS)

IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proinflammatory; serum levels of proinflammatory cytokines, C-reactive protein, and leptin and blood levels of reactive oxygen species and antioxidant enzymes were evaluated)

IT C-reactive protein
Interleukin 6
Reactive oxygen species
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serum levels of proinflammatory cytokines, C-reactive protein, and leptin and blood levels of reactive oxygen species and antioxidant enzymes were evaluated)

IT Combination chemotherapy
(α-lipoic acid, carbocysteine lysine salt, vitamin E, A, C combination was well tolerated, effective for clin. response and significantly increased LBM, decreased ROS, proinflammatory cytokines in advanced cancer patient with CACS/OS)

IT 11103-57-4, Vitamin A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(-lipoic acid, carbocysteine lysine salt, vitamin E, A, C combination was well tolerated, effective for clin. response and significantly increased LBM, decreased ROS, proinflammatory cytokines in advanced cancer patient with CACS/OS)

IT 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclooxygenase-2 inhibitor celecoxib was well tolerated, effective for clin. response and significantly increased LBM, appetite, reduced ROS, proinflammatory cytokines and improved quality of life in advanced cancer patient with CACS/OS)

IT 169590-42-5, Celebrex
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor celecoxib was well tolerated, effective for clin. response and significantly increased LBM, appetite, reduced ROS, proinflammatory cytokines and improved quality of life in advanced cancer patient with CACS/OS)

IT 71-58-9, Provera
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medroxiprogesterone acetate therapy was well tolerated, effective for clin. response and significantly increased LBM, appetite, reduced ROS, proinflammatory cytokines and improved quality of life in advanced

cancer patient with CACS/OS)
IT 6217-54-5, Docosahexaenoic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaconutritional enriched with n-3 fatty acids (docosahexaenoic acid) was well tolerated, effective for clin. response, increased LBM, reduced ROS, proinflammatory cytokines and improved life in advanced cancer patient with CACS/OS)
IT **10417-94-4, Eicosapentaenoic acid**
851541-58-7, ProSure
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaconutritional enriched with n-3 fatty acids (**eicosapentaenoic acid**) was well tolerated, effective for clin. response, increased LBM, reduced ROS, proinflammatory cytokines and improved life in advanced cancer patient with CACS/OS)
IT 7782-44-7D, Oxygen, reactive species 169494-85-3, Leptin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serum levels of proinflammatory cytokines, C-reactive protein, and leptin and blood levels of reactive oxygen species and antioxidant enzymes were evaluated)
IT 50-81-7, Vitamin C, biological studies 1200-22-2, Tiobec 1406-18-4, Vitamin E 49673-81-6, Fluifort
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-lipoic acid, carbocysteine lysine salt, vitamin E, A, C combination was well tolerated, effective for clin. response and significantly increased LBM, decreased ROS, proinflammatory cytokines in advanced cancer patient with CACS/OS)
RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD
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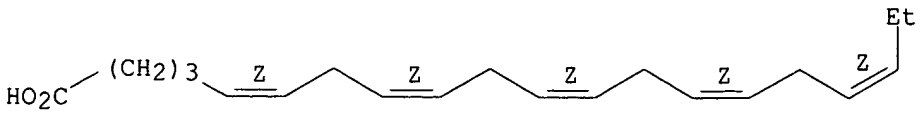
IT **10417-94-4, Eicosapentaenoic acid**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaconutritional enriched with n-3 fatty acids (**eicosapentaenoic acid**) was well tolerated, effective for clin. response, increased LBM, reduced ROS, proinflammatory cytokines and improved life in advanced cancer patient with CACS/OS)

RN 10417-94-4 HCAPLUS

CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX

NAME)

Double bond geometry as shown.



L46 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:644904 HCAPLUS
DN 141:349352
ED Entered STN: 11 Aug 2004
TI A pilot open case series of Ethyl-EPA supplementation in the treatment of **anorexia nervosa**
AU **Ayton, Agnes K.**; Azaz, Amer; **Horrobin, David F.**
CS Hull and East Riding Community NHS Trust, ST19 9QT, UK
SO Prostaglandins, Leukotrienes and Essential Fatty Acids (2004), 71(4), 205-209
CODEN: PLEAEU; ISSN: 0952-3278
PB Elsevier B.V.
DT Journal
LA English
CC 18-5 (Animal Nutrition)
AB **Anorexia nervosa** (AN) carries the highest risk of morbidity and mortality amongst psychiatric disorders. The efficacy of current treatment approaches is limited. Despite the fat-phobic nature of the disease, poly-unsatd. fatty acids (PUFAs) have not received much research attention. Patients who consume western diet, which is rich in n-6 PUFAs and trans-fatty acids, are likely to develop severe n-3 PUFA deficiency during self-induced starvation. Re-feeding programs do not take into consideration n-3 EFA intake, possibly leading to further n-3 PUFA deficiency during weight restoration, and this might contribute to the maintenance of the disorder. To test this hypothesis, we carried out a systematic case series of E-EPA supplementation in the treatment of AN. Seven young patients received 1 g/day E-EPA in addition to standard treatment, and were followed up for 3 mo. Three of them recovered and four improved. Randomized controlled trials are warranted to examine the effectiveness of E-EPA in AN further.
ST **eicosapentaenoate anorexia nervosa**
IT Appetite
(**anorexia nervosa**; fatty acid supplementation and **anorexia nervosa**)
IT **10417-94-4, Eicosapentaenoic acid**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fatty acid supplementation and **anorexia nervosa**)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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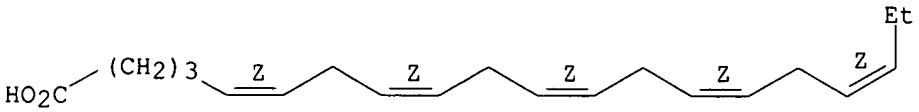
IT **10417-94-4, Eicosapentaenoic acid**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fatty acid supplementation and **anorexia nervosa**)
RN 10417-94-4 HCAPLUS
CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L46 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:317047 HCAPLUS
DN **141:105641**
ED Entered STN: 19 Apr 2004
TI Dietary polyunsaturated fatty acids and **anorexia nervosa** : Is there a link?
AU **Ayton, Agnes K.**
CS Consultant Child and Adolescent Psychiatrist, Eating Disorders Unit, Huntercombe Stafford Hospital, Staffordshire, ST19 9QT, UK
SO Nutritional Neuroscience (2004), 7(1), 1-12
CODEN: NNINFE; ISSN: 1028-415X
PB Taylor & Francis Ltd.
DT Journal; General Review
LA English
CC 18-0 (Animal Nutrition)
Section cross-reference(s): 14
AB A review. There has been little research examining the link between dietary fat intake and the symptoms and consequences of **anorexia nervosa**. In this selective literature review, the potential significance of poly-unsatd. fatty acids is discussed. It is hypothesised that dietary restriction causes essential fatty acid deficiencies and poly-unsatd. fatty acid abnormalities, which might contribute to the phys. and mental symptoms and the maintenance of the disorder. The examination of epidemiol., symptoms, co-morbidity, and consequences suggest that poly-unsatd. fatty acid and phospholipid abnormalities are significant in **anorexia nervosa**. This will be an important area for future research, and may lead to the development of new interventions.
ST review diet polyunsatd fatty acid **anorexia nervosa**
IT Appetite
(**anorexia nervosa**; dietary polyunsatd. fatty acids and **anorexia nervosa**)
IT Diet
Human
(dietary polyunsatd. fatty acids and **anorexia nervosa**)
IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polyunsatd., omega-3; dietary polyunsatd. fatty acids and

anorexia nervosa)
IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polyunsatd.; dietary polyunsatd. fatty acids and **anorexia nervosa**)
RE.CNT 144 THERE ARE 144 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L46 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2003:821113** HCAPLUS
DN 139:393945
ED Entered STN: 20 Oct 2003
TI Pathogenesis of cancer cachexia
AU Tisdale, Michael J.
CS Cancer Biochemistry at the Pharmaceutical Sciences Research Institute, Aston University, Birmingham, UK
SO Journal of Supportive Oncology (2003), 1(3), 159-168
CODEN: JSOOBY; ISSN: 1544-6794
PB BioLink Communications, Inc.
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
AB A review. Cachexia is a progressive wasting syndrome characterized by extensive loss of adipose tissue and skeletal muscle. It occurs in about half of all cancer patients. While **anorexia** also may be present, the energy deficit alone does not explain the pathogenesis of cachexia. The presence of an acute phase response (APR) has been linked to accelerated weight loss and a shortened survival time. The APR is thought to be initiated by cytokines such as interleukin (IL)-6 and IL-8, production of which is induced by a tumor factor, proteolysis inducing factor (PIF). Cachectic cancer patients also show an increased expression of uncoupling protein-3 in muscle, which may act as an energy sink, increasing energy expenditure. Loss of adipose tissue appears to be due to an increase in degradation of triglycerides, rather than a decrease in synthesis. One candidate for this effect is a tumor lipid mobilizing factor which stimulates lipolysis directly through a cAMP-mediated process via interaction with a β3-adrenergic receptor. Loss of skeletal muscle arises from both a depression in protein synthesis and an increase in protein degradation The major proteolytic pathway involved in intracellular protein breakdown in cachectic muscle is the ATP-ubiquitin-dependent proteolytic pathway. Both PIF and tumor necrosis factor-α, but not other cytokines, can induce expression of the key regulatory components of this pathway. **Eicosapentaenoic acid**, found in oily fish, effectively attenuates protein degradation in cachectic muscle by inhibiting the increased proteasome expression and can stabilize body weight in cachectic cancer patients.
ST review acute phase response interleukin TNF cytokine cancer cachexia; ubiquitin proteasome proteolysis energy metab cancer cachexia review; glyceride degrdn lipolysis **eicosapentaenoate** cancer cachexia review
IT Uncoupling protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(3; role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)
IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PIF (proteolysis-inducing factor); role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)

IT **Cachexia**
(cancerous; role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)

IT Glycerides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(degradation of; role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)

IT Acute-phase response
Energy metabolism, animal
Human
Translation, genetic
(role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)

IT Interleukin 6
Interleukin 8
Lipolysis
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)

IT Protein degradation
(ubiquitination; role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)

IT **10417-94-4, Eicosapentaenoic acid**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**eicosapentaenoic acid** as promising new treatment of cancer cachexia)

IT 56-65-5, 5'-ATP, biological studies 60267-61-0, Ubiquitin 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of acute-phase response, cytokines, hypermetabolism, energy expenditure, and ubiquitin proteasome proteolytic pathway in pathogenesis of cancer cachexia)

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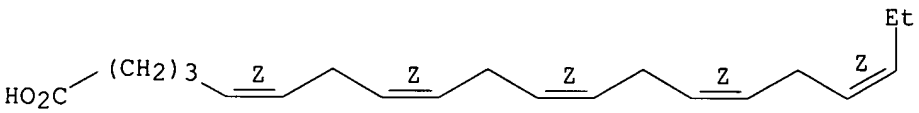
IT **10417-94-4, Eicosapentaenoic acid**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**eicosapentaenoic acid** as promising new treatment of cancer cachexia)
RN 10417-94-4 HCAPLUS
CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L46 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2001:373862** HCAPLUS
DN 136:51818
ED Entered STN: 24 May 2001
TI Cancer **anorexia** and cachexia
AU Tisdale, M. J.
CS Pharmaceutical Sciences Research Institute, Aston University, Birmingham, UK
SO Nutrition (New York, NY, United States) (2001), 17(5), 438-442
CODEN: NUTRER; ISSN: 0899-9007
PB Elsevier Science Inc.
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
AB A review. Patients with cancer cachexia experience a profound wasting of adipose tissue and lean body mass. **Anorexia**, although often present, is insufficient to account for tissue wasting because (1) cachexia involves massive depletion of skeletal muscle that does not occur during **anorexia**, (2) nutritional supplementation cannot replenish the loss of lean body mass, (3) cachexia can occur without **anorexia**, and (4) food intake might be normal for the lower weight of the cancer patient. **Anorexia** can arise from (1) decreased taste and smell of food, (2) early satiety, (3) dysfunctional hypothalamic membrane adenylate cyclase, (4) increased brain tryptophan, and (5) cytokine production Appetite stimulants such as cyproheptadine,

medroxyprogesterone acetate, and megestrol acetate do not significantly improve lean body mass. Tumor products might be more important in the development of cachexia. Cachectic patients excrete in their urine a lipid-mobilizing factor that directly stimulates lipolysis in a cAMP-dependent manner and increases energy expenditure. Loss of skeletal muscle in cachexia is caused by upregulation of the ubiquitin-proteasome catabolic pathway. Cachexia-inducing tumors elaborate a sulfated glycoprotein, which directly initiates protein catabolism in skeletal muscle. The action of this proteolysis-inducing factor is attenuated by the polyunsatd. fatty acid **eicosapentaenoic acid**, which is also effective in preventing loss of skeletal muscle in cancer patients. Antagonists of tumor catabolic factors will provide important new agents in the treatment of cancer cachexia.

ST review protein metab feeding cancer **anorexia** cachexia; fatty acid **eicosapentaenoate** cancer cachexia **anorexia** review; adipose tissue muscle metab anticachectic cancer **anorexia** cachexia review

IT **Cachexia**
(cancerous, anticachectics; pathogenesis and treatment of cancer **anorexia** and cachexia)

IT Metabolism
(catabolic, of proteins; pathogenesis and treatment of cancer **anorexia** and cachexia)

IT **Body weight**
(**loss**; pathogenesis and treatment of cancer **anorexia** and cachexia)

IT Adipose tissue
(metabolism; pathogenesis and treatment of cancer **anorexia** and cachexia)

IT **Anorexia**
Energy metabolism, animal
Feeding
Muscle
(pathogenesis and treatment of cancer **anorexia** and cachexia)

IT Protein metabolism
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pathogenesis and treatment of cancer **anorexia** and cachexia)

IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd.; pathogenesis and treatment of cancer **anorexia** and cachexia)

IT **10417-94-4, Eicosapentaenoic acid**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pathogenesis and treatment of cancer **anorexia** and cachexia)

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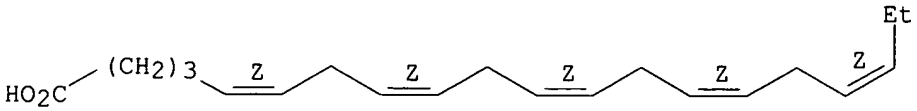
IT **10417-94-4, Eicosapentaenoic acid**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pathogenesis and treatment of cancer **anorexia** and cachexia)
RN 10417-94-4 HCAPLUS
CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L46 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2000:856297** HCAPLUS
DN 134:264084
ED Entered STN: 07 Dec 2000
TI Metabolic abnormalities in cachexia and **anorexia**
AU Tisdale, Michael J.
CS Pharmaceutical Sciences Research Institute, Aston University, Birmingham, UK
SO Nutrition (New York) (2000), 16(10), 1013-1014
CODEN: NUTRER; ISSN: 0899-9007
PB Elsevier Science Inc.
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
AB A review with 34 refs. An increased glucose requirement by many solid tumors produces an increased metabolic demand on the liver, resulting in an increased energy expenditure. In addition, several cytokines and tumor catabolic products have been suggested as being responsible for the depletion of adipose tissue and skeletal-muscle mass in cachexia. A sulfated glycoprotein of mol. mass 24 kDa, produced by cachexia-inducing tumors and present in the urine of cancer patients actively losing weight, has been shown to be capable of inducing direct muscle catabolism in vitro and a state of cachexia in vivo, with specific loss of the non-fat carcass mass. In vitro studies have shown the bioactivity of this proteolysis-inducing factor to be attenuated by the polyunsatd. fatty acid, **eicosapentaenoic acid**. Preliminary clin. studies have shown that **eicosapentaenoic acid** stabilizes body weight and protein and fat reserves in patients with pancreatic carcinoma. Further trials are required to confirm the efficacy of **eicosapentaenoic acid** and to determine the anticachectic activity in other types of cancer.
ST review metabolic abnormality cachexia **anorexia**
IT **Cachexia**
(cancerous; metabolic abnormalities in cachexia and **anorexia** in humans and laboratory animals)

IT Metabolism, animal
(disorder; metabolic abnormalities in cachexia and **anorexia** in humans and laboratory animals)
IT **Anorexia**
(metabolic abnormalities in cachexia and **anorexia** in humans and laboratory animals)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L46 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2000:415524** HCAPLUS
DN 133:22406
ED Entered STN: 22 Jun 2000
TI Method for the prevention and treatment of cachexia and **anorexia**
IN Abbruzzese, Bonnie Chandler; McCamish, Mark Anthony; Cope, Frederick Oliver; Demichele, Stephen Joseph
PA Abbott Laboratories, USA
SO U.S., 12 pp., Cont.-in-part of U. S. Ser. No. 635,179, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A23J0003-16
ICS A61K0038-17
INCL 514021000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 17, 18

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6077828	A	20000620	US 1997-842454	19970424
	CA 2252513	AA	19971030	CA 1997-2252513	19970425
	CA 2252513	C	20021119		
	CA 2355247	AA	19971030	CA 1997-2355247	19970425
	CA 2355247	C	20021126		
	WO 9739749	A2	19971030	WO 1997-US6897	19970425
	WO 9739749	A3	19971204		
	W: AU, CA, JP, MX, NZ				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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	AU 716532	B2	20000224		
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	PT 914111	T	20040430	PT 1997-921367	19970425
	EP 1415650	A1	20040506	EP 2003-26561	19970425
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	ES 2210523	T3	20040701	ES 1997-921367	19970425
	MX 9808867	A	20000531	MX 1998-8867	19981023
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PRAI	US 1996-635179	B2	19960425		
	US 1997-842454	A	19970424		
	CA 1997-2252513	A3	19970425		
	EP 1997-921367	A3	19970425		
	NZ 1997-332291	A1	19970425		
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	US 2000-479550	A1	20000107		
	US 2000-642630	A1	20000818		
	US 2001-2179	A1	20011205		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6077828	ICM	A23J0003-16
	ICS	A61K0038-17
	INCL	514021000
	IPCI	A23J0003-16 [ICM,7]; A61K0038-17 [ICS,7]
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CA 2355247	IPCI	A61K0031-20 [ICM,7]; A61K0031-015 [ICS,7]; A61K0033-04 [ICS,7]; A61P0003-04 [ICS,7]; A23L0001-302 [ICS,7]; A61K0031-355 [ICS,7]; A61K0031-375 [ICS,7]

WO 9739749	IPCI	A61K0031-20 [ICM,6]
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MX 9808867	IPCI	A61K0031-20 [ICM,5]
HK 1019857	IPCI	A61K [ICM,7]; A61P [ICS,7]
US 6326355	IPCI	A23J0003-16 [ICM,7]; A61K0038-17 [ICS,7]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
	NCL	514/021.000; 424/523.000; 426/072.000; 426/601.000; 426/602.000; 426/656.000; 426/800.000; 426/801.000; 514/578.000; 514/725.000; 514/730.000; 514/739.000
	ECLA	A23L001/29F; A23L001/30C2; A23L001/304; A23L001/305A
US 6387883	IPCI	A23J0003-16 [ICM,7]; A61K0038-17 [ICS,7]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
	NCL	514/021.000; 424/523.000; 426/072.000; 426/601.000; 426/602.000; 426/656.000; 426/800.000; 426/801.000; 514/578.000; 514/725.000; 514/730.000; 514/739.000
	ECLA	A23L001/29F; A23L001/30C2; A23L001/304; A23L001/305A

US 2002099020 IPCI A61K0038-00 [ICM,7]; A61K0031-355 [ICS,7]; A61K0031-375 [ICS,7]; A61K0031-015 [ICS,7]; A61K0033-04 [ICS,7]
IPCR A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
NCL 514/021.000
ECLA A23L001/29F; A23L001/30C2; A23L001/304; A23L001/305A
US 2004167081 IPCI A61K0031-70 [ICM,7]; A61K0031-20 [ICS,7]
IPCR A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
NCL 514/023.000
ECLA A23L001/29F; A23L001/30C2; A23L001/304; A23L001/305A

AB The present invention relates to methods and nutritional compns. for the prevention and treatment of cachexia and **anorexia**. The methods of the invention comprise administering a composition comprising effective amts. of ω-3 fatty acids such as alpha-linolenic acid, stearidonic acid, **eicosapentaenoic acid**, docosapentaenoic acid, docosahexaenoic acid or mixts. thereof; of branched-chain amino acids valine, leucine, isoleucine or mixts. thereof, with or without reduced levels of tryptophan and 5-hydroxytryptophan, and of an antioxidant system selected from the group comprising beta-carotene, vitamin C, vitamin E, selenium, or mixts. thereof.

ST diet therapeutic **anorexia** cachexia

IT Amino acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(branched; therapeutic diet for prevention and treatment of cachexia and **anorexia**)

IT Fats and Glyceridic oils, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fish; therapeutic diet for prevention and treatment of cachexia and **anorexia**)

IT Glycerides, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medium-chain; therapeutic diet for prevention and treatment of cachexia and **anorexia**)

IT Fatty acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., omega-3; therapeutic diet for prevention and treatment of cachexia and **anorexia**)

IT Fatty acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., omega-6; therapeutic diet for prevention and treatment of cachexia and **anorexia**)

IT Lecithins
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soya; therapeutic diet for prevention and treatment of cachexia and **anorexia**)

IT **Anorexia**
Antioxidants
Cachexia
(therapeutic diet for prevention and treatment of cachexia and

anorexia)
IT Canola oil
Lecithins
Soybean oil
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic diet for prevention and treatment of cachexia and **anorexia**)
IT Diet
(therapeutic; therapeutic diet for prevention and treatment of cachexia and **anorexia**)
IT 50-81-7, Vitamin C, biological studies 61-90-5, L-Leucine, biological studies 72-18-4, L-Valine, biological studies 73-32-5, L-Isoleucine, biological studies 463-40-1, α-Linolenic acid 1406-18-4, Vitamin E 6217-54-5, Cervonic acid 7235-40-7, β-Carotene 7782-49-2, Selenium, biological studies **10417-94-4**, **Timnodonic acid** 20290-75-9, Stearidonic acid 32839-34-2, Docosapentaenoic acid
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic diet for prevention and treatment of cachexia and **anorexia**)
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(4) Anon; EP 0462398 1991 HCAPLUS
(5) Anon; WO 9508349 1995 HCAPLUS
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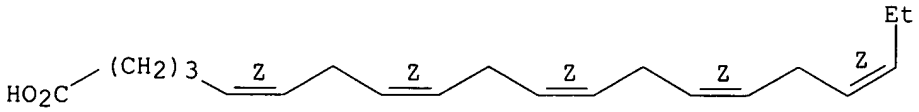
IT **10417-94-4, Timnodonic acid**
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic diet for prevention and treatment of cachexia and **anorexia**)
RN 10417-94-4 HCAPLUS
CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L46 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **1999:61519** HCAPLUS
DN 130:222473
ED Entered STN: 01 Feb 1999
TI Wasting in cancer
AU Tisdale, Michael J.
CS Pharmaceutical Sciences Institute, Aston University, Birmingham, B4 7ET, UK
SO Journal of Nutrition (1999), 129(1S), 243S-246S
CODEN: JONUAI; ISSN: 0022-3166
PB American Society for Nutritional Sciences
DT Journal; General Review
LA English
CC 18-0 (Animal Nutrition)
Section cross-reference(s): 14
AB A review with 47 refs. Progressive weight loss is a common feature of many types of cancer and is responsible not only for a poor quality of life and poor response to chemotherapy, but also a shorter survival time than is found in patients with comparable tumors without weight loss. Although **anorexia** is common, a decreased food intake alone is unable to account for the changes in body composition seen in cancer patients, and increasing nutrient intake is unable to reverse the wasting syndrome. Although energy expenditure is increased in some patients, cachexia can occur even with a normal energy expenditure. Various factors have been investigated as mediators of tissue wasting in cachexia. These include cytokines such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interferon-γ (IFN-γ) and leukemia

inhibitory factor (LIF), as well as tumor-derived factors such as lipid mobilizing factor (LMF) and protein mobilizing factor (PMF), which can directly mobilize fatty acids and amino acids from adipose tissue and skeletal muscle resp. Induction of lipolysis by the cytokines is thought to result from an inhibition of lipoprotein lipase (LPL), although clin. studies provide no evidence for an inhibition of LPL in the adipose tissue of cancer patients. Instead there is an increased expression of hormone sensitive lipase, the enzyme activated by LMF. Protein degradation in cachexia is associated with an increased activity of the ATP-ubiquitin-proteasome pathway. The biol. activity of both the LMF and PMF was shown to be attenuated by **eicosapentaenoic acid** (EPA).
Clin. studies show that this polyunsatd. fatty acid is able to stabilize the rate of weight loss and adipose tissue and muscle mass in cachectic patients with unresectable pancreatic cancer. Knowledge of the mechanism of cancer cachexia should lead to the development of new therapeutic agents.

ST review cancer wasting cachexia

IT **Cachexia**
(cancerous; factors mediating wasting in cancer)

IT Diet
Energy metabolism, animal
(factors mediating wasting in cancer in relation to)

IT Disease, animal
(wasting; factors mediating wasting in cancer)

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L46 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **1997:717812** HCAPLUS
DN 127:362629
ED Entered STN: 13 Nov 1997
TI Method for the prevention and treatment of cachexia and **anorexia**
IN Abbruzzese, Bonnie Chandler; McCamish, Mark Anthony; Cope, Frederick Oliver; Demichele, Stephen Joseph
PA Abbott Laboratories, USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K0031-20
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 18
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9739749	A2	19971030	WO 1997-US6897	19970425
	WO 9739749	A3	19971204		
	W: AU, CA, JP, MX, NZ				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6077828	A	20000620	US 1997-842454	19970424
	AU 9727424	A1	19971112	AU 1997-27424	19970425
	AU 716532	B2	20000224		
	EP 914111	A2	19990512	EP 1997-921367	19970425
	EP 914111	B1	20031119		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	JP 11508282	T2	19990721	JP 1997-538345	19970425
	NZ 332291	A	20000728	NZ 1997-332291	19970425
	AT 254454	E	20031215	AT 1997-921367	19970425
	MX 9808867	A	20000531	MX 1998-8867	19981023
	HK 1019857	A1	20041105	HK 1999-105140	19991109
PRAI	US 1996-635179	A	19960425		
	US 1997-842454	A	19970424		
	WO 1997-US6897	W	19970425		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9739749	ICM	A61K0031-20
	IPCI	A61K0031-20 [ICM,6]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
	ECLA	A23L001/29F; A23L001/30C2; A23L001/304; A23L001/305A

US 6077828	IPCI	A23J0003-16 [ICM,7]; A61K0038-17 [ICS,7]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
	NCL	514/021.000; 424/523.000; 426/072.000; 426/601.000; 426/602.000; 426/656.000; 426/800.000; 426/801.000; 514/578.000; 514/725.000; 514/730.000; 514/739.000
	ECLA	A23L001/29F; A23L001/30C2; A23L001/304; A23L001/305A
AU 9727424	IPCI	A61K0031-20 [ICM,6]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
EP 914111	IPCI	A61K0031-20 [ICM,6]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
JP 11508282	IPCI	A61K0031-20 [ICM,6]; A61K0031-015 [ICS,6]; A61K0031-195 [ICS,6]; A61K0031-355 [ICS,6]; A61K0031-375 [ICS,6]; A61K0033-04 [ICS,6]; A61K0045-00 [ICS,6]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
NZ 332291	IPCI	A61K0031-20 [ICM,7]
	IPCR	A23L0001-29 [I,A]; A23L0001-29 [I,C]; A23L0001-30 [I,A]; A23L0001-30 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A23L0001-305 [I,A]; A23L0001-305 [I,C]
AT 254454	IPCI	A61K0031-20 [ICM,7]; A61P0003-04 [ICS,7]
MX 9808867	IPCI	A61K0031-20 [ICM,5]
HK 1019857	IPCI	A61K [ICM,7]; A61P [ICS,7]

AB The present invention relates to methods and nutritional compns. for the prevention and treatment of cachexia and **anorexia**. The methods comprise administering a composition containing effective amts. of (1) ω-3 fatty acids, such as α-linolenic acid, stearidonic acid, **eicosapentaenoic acid**, docosapentaenoic acid, docosahexaenoic acid or mixts. thereof, (2) branched-chain amino acids, such as valine, leucine, isoleucine or mixts. thereof, with or without reduced levels of tryptophan and 5-hydroxytryptophan, and (3) antioxidant system selected from the group comprising β-carotene, vitamin C, vitamin E, selenium, or mixts. thereof.

ST enteral nutrient antioxidant **anorexia** cachexia

IT Amino acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(branched; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT **Anorexia**
Cachexia
Immunostimulants
(enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Canola oil
Soybean oil
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteral compns. containing oil blend and amino acids and antioxidants for

treatment of cachexia and **anorexia**)

IT Nutrients
(enteral; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Drug delivery systems
(enteric; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Fats and Glyceridic oils, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fish; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Antitumor agents
(for enhancing transport and efficacy; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Glycerides, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medium-chain; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Fatty acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., n-3; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Fatty acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., omega-6; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT Lecithins
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soya; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT 73-22-3, L-Tryptophan, biological studies 4350-09-8, L-5-HydroxyTryptophan
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(at limited amount; enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

IT 50-81-7, Vitamin C, biological studies 61-90-5, L-Leucine, biological studies 72-18-4, L-Valine, biological studies 73-32-5, L-Isoleucine, biological studies 463-40-1 1406-18-4, Vitamin E 6217-54-5, Docosahexaenoic acid 7235-40-7, β-Carotene 7782-49-2, Selenium, biological studies **10417-94-4, Eicosapentaenoic acid** 20290-75-9, Stearidonic acid 32839-34-2, Docosapentaenoic acid
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

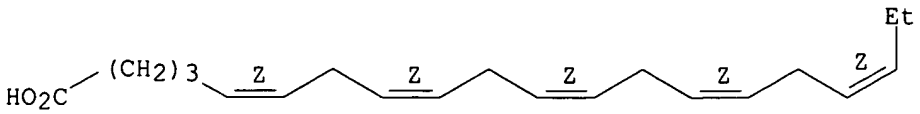
IT **10417-94-4, Eicosapentaenoic acid**
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteral compns. containing oil blend and amino acids and antioxidants for treatment of cachexia and **anorexia**)

RN 10417-94-4 HCAPLUS

CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX

NAME)

Double bond geometry as shown.



L46 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **1993:514455** HCAPLUS
DN 119:114455
ED Entered STN: 18 Sep 1993
TI Cancer cachexia
AU Tisdale, M. J.
CS Pharm. Sci. Inst., Aston Univ., Birmingham, B4 7ET, UK
SO Anti-Cancer Drugs (1993), 4(2), 115-25
CODEN: ANTDEV; ISSN: 0959-4973
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
AB A review with 102 refs. Cachexia is a common problem in the clin. management of cancer patients, particularly those with solid tumors. Cachexia is manifested as weight loss with a massive depletion of both adipose tissues and muscle mass, and death is probably due to the loss of lean body tissue. The survival time is shorter in patients with cachexia and the responses to chemotherapy are also reduced. Although **anorexia** frequently accompanies cachexia, attempts to halt or reverse cachexia by nutritional repletion have not been successful. The cancer cachexia may be due to metabolic abnormalities produced by the tumor in addition to the underlying **anorexia**. In some patients the weight loss is associated with an increased relative energy expenditure, possibly through an elevated adrenergic state. Several factors have been postulated as mediators of cancer cachexia and can include substances with hormone-like characteristics which cause direct catabolism of host tissues or cytokines which cause alterations in host metabolism indirectly. There are the conventional catabolic hormones and a lipid-mobilizing factor (LMF) produced by tumors which cause a direct breakdown of the adipose tissue. Tumor necrosis factor-α, interleukin-6, interferon-γ, and leukemia inhibitory factor are examples of possibly cachexia-related cytokines. The substances may influence the adipose tissue indirectly through an inhibition of lipoprotein lipase. The reversal of cachexia has been achieved by agents stimulating food intake, e.g. megestrol acetate, or directly inhibiting LMF, e.g. **eicosapentaenoic acid** . While agents in the first group can stimulate tumor growth, those in the second group act as tumor growth inhibitors. The products of catabolism of host tissues may be important for tumor growth and chemotherapeutic intervention.
ST review cancer cachexia mechanism
IT Neoplasm
(cachexia in humans with, mechanisms of)
IT **Cachexia**
(in cancer, mechanisms of, in humans)

=> => fil medline
FILE 'MEDLINE' ENTERED AT 11:30:07 ON 10 MAY 2006

FILE LAST UPDATED: 9 MAY 2006 (20060509/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d his l56-

     (FILE 'REGISTRY' ENTERED AT 11:24:39 ON 10 MAY 2006)

     FILE 'HCAPLUS' ENTERED AT 11:24:51 ON 10 MAY 2006

     FILE 'MEDLINE' ENTERED AT 11:26:18 ON 10 MAY 2006
L56         2311 S L9 OR L10 OR L50 OR L34 OR L35
L57         3876 S L4 OR L12
L58         3877 S L56,L57
L59        21444 S L19 OR L21
                 E ANOREXIA/CT
                 E E3+ALL
L60         2730 S E5+NT
                 E E8+ALL
L61         7839 S E4+NT
                 E E3+ALL
L62        14422 S E3+NT
                 E BULIMIA/CT
                 E E3+ALL
L63         4008 S E6+NT OR E11+NT
L64           22 S L58 AND L59-L63
L65            9 S L64 AND PY<=2002
L66           13 S L64 NOT L65
L67            3 S L66 AND 2003/PY
L68           12 S L65,L67

     FILE 'MEDLINE' ENTERED AT 11:30:07 ON 10 MAY 2006

=> d all tot 168

L68  ANSWER 1 OF 12     MEDLINE on STN
AN   2004429536     MEDLINE
DN   PubMed ID: 15334872
TI   Pathogenesis of cancer cachexia.
AU   Tisdale Michael J
CS   Pharmaceutical Sciences Research Institute, Aston University, Aston
     Triangle, Birmingham, United Kingdom.. m.j.tisdale@aston.ac.uk
SO   The journal of supportive oncology, (2003 Sep-Oct) Vol. 1, No.
```

3, pp. 159-68. Ref: 62
Journal code: 101181305. ISSN: 1544-6794.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200410
ED Entered STN: 1 Sep 2004
Last Updated on STN: 29 Oct 2004
Entered Medline: 28 Oct 2004
AB Cachexia is a progressive wasting syndrome characterized by extensive loss of adipose tissue and skeletal muscle. It occurs in about half of all cancer patients. While **anorexia** also may be present, the energy deficit alone does not explain the pathogenesis of cachexia. The presence of an acute phase response (APR) has been linked to accelerated weight loss and a shortened survival time. The APR is thought to be initiated by cytokines such as interleukin (IL)-6 and IL-8, production of which is induced by a tumor factor, proteolysis inducing factor (PIF). Cachectic cancer patients also show an increased expression of uncoupling protein-3 in muscle, which may act as an energy sink, increasing energy expenditure. Loss of adipose tissue appears to be due to an increase in degradation of triglycerides, rather than a decrease in synthesis. One candidate for this effect is a tumor lipid mobilizing factor, which stimulates lipolysis directly through a cyclic AMP-mediated process via interaction with a beta3-adrenergic receptor. Loss of skeletal muscle arises from both a depression in protein synthesis and an increase in protein degradation. The major proteolytic pathway involved in intracellular protein breakdown in cachectic muscle is the ATP-ubiquitin-dependent proteolytic pathway. Both PIF and tumor necrosis factor-alpha, but not other cytokines, can induce expression of the key regulatory components of this pathway. **Eicosapentaenoic acid**, found in oily fish, effectively attenuates protein degradation in cachectic muscle by inhibiting the increased proteasome expression and can stabilize body weight in cachectic cancer patients.
CT Adipose Tissue: DE, drug effects
Adipose Tissue: PP, physiopathology
Cachexia: DT, drug therapy
Cachexia: ET, etiology
*Cachexia: PP, physiopathology
Cytokines: PH, physiology
Dietary Supplements
Disease Progression
Eicosapentaenoic Acid: PD, pharmacology
Eicosapentaenoic Acid: TU, therapeutic use
Energy Metabolism: PH, physiology
Humans
Muscle, Skeletal: DE, drug effects
Muscle, Skeletal: PP, physiopathology
Neoplasms: CO, complications
*Neoplasms: PP, physiopathology
Weight Loss: DE, drug effects
RN **1553-41-9 (Eicosapentaenoic Acid)**
CN 0 (Cytokines)

L68 ANSWER 2 OF 12 MEDLINE on STN
AN 2003591984 MEDLINE
DN PubMed ID: 14673061
TI **Eicosapentaenoic acid** as a targeted therapy for cancer cachexia.

AU Belda-Iniesta Cristobal; de Castro Carpeno Javier; Fresno Vara Juan Angel; Cejas Guerrero Paloma; Casado Saenz Enrique; Espinosa Arranz Enrique; Redondo Sanchez Andres; Feliu Battle Jaime; Gonzalez Baron Manuel
SO Journal of clinical oncology : official journal of the American Society of Clinical Oncology, **(2003 Dec 15)** Vol. 21, No. 24, pp. 4657-8; author reply 4658.
Journal code: 8309333. ISSN: 0732-183X.
CM Comment on: J Clin Oncol. 2003 Jan 1;21(1):129-34. PubMed ID: 12506181
CY United States
DT Commentary
Letter
LA English
FS Priority Journals
EM 200402
ED Entered STN: 16 Dec 2003
Last Updated on STN: 14 Feb 2004
Entered Medline: 13 Feb 2004
CT Animals
Anorexia: ET, etiology
***Anorexia: TH, therapy**
Cachexia: ET, etiology
*Cachexia: TH, therapy
*Dietary Supplements
*Eicosanoic Acids: TU, therapeutic use
*Fish Oils: TU, therapeutic use
Humans
*Neoplasms: CO, complications
CN 0 (Eicosanoic Acids); 0 (Fish Oils)

L68 ANSWER 3 OF 12 MEDLINE on STN
AN 2002741916 MEDLINE
DN PubMed ID: 12506181
TI Effect of fish oil on appetite and other symptoms in patients with advanced cancer and **anorexia**/cachexia: a double-blind, placebo-controlled study.
AU Bruera Eduardo; Strasser Florian; Palmer J Lynn; Willey Jie; Calder Kathryn; Amyotte Gail; Baracos Vickie
CS Department of Palliative Care and Rehabilitation Medicine, The University of Texas M.D. Anderson Cancer Center, Houston, TX 77030-0049, USA.. ebruera@mail.mdanderson.org
SO Journal of clinical oncology : official journal of the American Society of Clinical Oncology, **(2003 Jan 1)** Vol. 21, No. 1, pp. 129-34.
Journal code: 8309333. ISSN: 0732-183X.
CM Comment in: J Clin Oncol. 2003 Dec 15;21(24):4657-8; author reply 4658. PubMed ID: 14673061
Comment in: J Clin Oncol. 2003 Sep 15;21(18):3545; author reply 3545-6. PubMed ID: 12972541
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 31 Dec 2002
Last Updated on STN: 16 Jan 2003
Entered Medline: 15 Jan 2003
AB PURPOSE: To determine whether high doses of fish oil, administered over 2 weeks, improve symptoms in patients with advanced cancer and decreased weight and appetite. PATIENTS AND METHODS: Sixty patients were randomly

assigned to fish oil capsules or placebo. Appetite, tiredness, nausea, well-being, caloric intake, nutritional status, and function were prospectively assessed at days 1 and 14. RESULTS: The baseline weight loss was 16 +/- 11 and 16 +/- 8 kg in the fish oil (n = 30) and placebo (n = 30) group respectively, whereas the baseline appetite (0 mm = best and 10 mm = worst) was 58 +/- 24 mm and 67 +/- 19 mm, respectively (P = not significant). The mean daily dose was 10 +/- 4 (fish oil group) and 9 +/- 3 (placebo group) capsules, which provided 1.8 g of **eicosapentaenoic acid** and 1.2 g of docosahexaenoic acid in the fish oil group. No significant differences in symptomatic or nutritional parameters were found (P <.05), and there was no correlation between changes in different variables between days 1 and 14 and the fish oil doses. Finally, the majority of the patients were not able to swallow more than 10 fish oil capsules per day, mainly because of burping and aftertaste. CONCLUSION: Fish oil did not significantly influence appetite, tiredness, nausea, well-being, caloric intake, nutritional status, or function after 2 weeks compared with placebo in patients with advanced cancer and loss of both weight and appetite.

CT Check Tags: Female; Male
Anorexia: ET, etiology
***Anorexia: TH, therapy**
Cachexia: ET, etiology
*Cachexia: TH, therapy
*Dietary Supplements
Double-Blind Method
*Fish Oils: TU, therapeutic use
Humans
Middle Aged
*Neoplasms: CO, complications
Research Support, Non-U.S. Gov't
Statistics, Nonparametric

CN 0 (Fish Oils)

L68 ANSWER 4 OF 12 MEDLINE on STN
AN 2002655005 MEDLINE
DN PubMed ID: 12415256
TI Cachexia in cancer patients.
AU Tisdale Michael J
CS Pharmaceutical Sciences Research Institute, Aston University, Birmingham B4 7ET, UK.. m.j.tisdale@aston.ac.uk
SO Nature reviews. Cancer, **(2002 Nov)** Vol. 2, No. 11, pp. 862-71.
Ref: 94
Journal code: 101124168. ISSN: 1474-175X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200212
ED Entered STN: 5 Nov 2002
Last Updated on STN: 18 Dec 2002
Entered Medline: 13 Dec 2002
CT Acute-Phase Proteins: ME, metabolism
Adipose Tissue: ME, metabolism
Animals
Anorexia: CI, chemically induced
Anorexia: ET, etiology
Anorexia: ME, metabolism
Body Composition
*Cachexia

Cachexia: DT, drug therapy
Cachexia: ET, etiology
Cachexia: ME, metabolism
Carrier Proteins: PH, physiology
Comparative Study
Cysteine Endopeptidases: ME, metabolism
Cytokines: PH, physiology
Eicosapentaenoic Acid: TU, therapeutic use
Energy Intake
Energy Metabolism
Fish Oils: TU, therapeutic use
Humans
Hypothalamus: PP, physiopathology
Lipolysis
Multienzyme Complexes: ME, metabolism
Muscle Proteins: ME, metabolism
Muscle, Skeletal: ME, metabolism
Neoplasm Proteins: PH, physiology
*Neoplasms: CO, complications
Neoplasms: ME, metabolism
Neuropeptides: PH, physiology
Proteasome Endopeptidase Complex
Rats
Ubiquitin: ME, metabolism
Weight Loss

RN **1553-41-9 (Eicosapentaenoic Acid)**
CN 0 (Acute-Phase Proteins); 0 (Carrier Proteins); 0 (Cytokines); 0 (Fish Oils); 0 (Multienzyme Complexes); 0 (Muscle Proteins); 0 (Neoplasm Proteins); 0 (Neuropeptides); 0 (Ubiquitin); 0 (mitochondrial uncoupling protein 3); EC 3.4.22 (Cysteine Endopeptidases); EC 3.4.25.1 (Proteasome Endopeptidase Complex)

L68 ANSWER 5 OF 12 MEDLINE on STN
AN 2002011631 MEDLINE
DN PubMed ID: 11377146
TI Cancer **anorexia** and cachexia.
AU Tisdale M J
CS Pharmaceutical Sciences Research Institute, Aston University, Birmingham, United Kingdom.
SO Nutrition (Burbank, Los Angeles County, Calif.), **(2001 May)** Vol. 17, No. 5, pp. 438-42. Ref: 80
Journal code: 8802712. ISSN: 0899-9007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200201
ED Entered STN: 21 Jan 2002
Last Updated on STN: 25 Jan 2002
Entered Medline: 3 Jan 2002
AB Patients with cancer cachexia experience a profound wasting of adipose tissue and lean body mass. **Anorexia**, although often present, is insufficient to account for tissue wasting because 1) cachexia involves massive depletion of skeletal muscle that does not occur during **anorexia**, 2) nutritional supplementation cannot replenish the loss of lean body mass, 3) cachexia can occur without **anorexia**, and 4) food intake might be normal for the lower weight of the cancer patient. **Anorexia** can arise from 1) decreased taste and smell of food, 2) early satiety, 3) dysfunctional hypothalamic membrane adenylate cyclase,

4) increased brain tryptophan, and 5) cytokine production. Appetite stimulants such as cyproheptadine, medroxyprogesterone acetate, and megestrol acetate do not significantly improve lean body mass. Tumor products might be more important in the development of cachexia. Cachectic patients excrete in their urine a lipid-mobilizing factor that directly stimulates lipolysis in a cyclic AMP-dependent manner and increases energy expenditure. Loss of skeletal muscle in cachexia is caused by upregulation of the ubiquitin-proteasome catabolic pathway. Cachexia-inducing tumors elaborate a sulfated glycoprotein, which directly initiates protein catabolism in skeletal muscle. The action of this proteolysis-inducing factor is attenuated by the polyunsaturated fatty acid **eicosapentaenoic acid**, which is also effective in preventing loss of skeletal muscle in cancer patients. Antagonists of tumor catabolic factors will provide important new agents in the treatment of cancer cachexia.

CT ***Anorexia: ET, etiology**
Anorexia: ME, metabolism
Anorexia: TH, therapy
Appetite Stimulants: TU, therapeutic use
Blood Proteins: ME, metabolism
*Cachexia: ET, etiology
Cachexia: ME, metabolism
Cachexia: TH, therapy
Eicosanoic Acids: TU, therapeutic use
Humans
Lipid Metabolism
*Muscle, Skeletal: ME, metabolism
Neoplasms: ME, metabolism
*Neoplasms: PP, physiopathology
Peptides: ME, metabolism
Proteins: ME, metabolism
Research Support, Non-U.S. Gov't

CN 0 (Appetite Stimulants); 0 (Blood Proteins); 0 (Eicosanoic Acids); 0 (Peptides); 0 (Proteins); 0 (lipid mobilizing substance); 0 (proteolysis-inducing peptide)

L68 ANSWER 6 OF 12 MEDLINE on STN
AN 2001667143 MEDLINE
DN PubMed ID: 11712791
TI Malnutrition and cachexia in ovarian cancer patients: pathophysiology and management.
AU Gadducci A; Cosio S; Fanucchi A; Genazzani A R
CS Department of Procreative Medicine, University of Pisa, Italy.. a.gadducci@obgyn.med.unipi.it
SO Anticancer research, **(2001 Jul-Aug)** Vol. 21, No. 4B, pp. 2941-7.
Ref: 92
Journal code: 8102988. ISSN: 0250-7005.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 10 Dec 2001
AB In ovarian cancer patients the poor nutritional status and cachexia are caused by the metabolic effects of the enlarging tumor masses and bowel obstruction. These patients may have a high resting energy expenditure due to increase in Cori cycle activity, glucose and triglyceride-fatty

acid cycling and gluconeogenesis. Biochemical mediators of cachexia include cytokines, such as tumor necrosis factor and interleukin-6, and tumor-produced catabolic factors, such as lipid-mobilizing factor, proteolysis-inducing factor, and anemia-inducing factor. Mechanisms involved in the pathogenesis of obstruction may include extrinsic occlusion of the bowel due to pelvic, mesenteric omental masses, or intestinal motility disorders due to infilor tration of the mesentery or bowel muscle and nerves. The relief of malnutrition and cachexia may be attempted through nutritional support, pharmacological approach (megestrol acetate, cyclooxygenase inhibitors) and palliative treatment of bowel obstruction. Very few agents have been demonstrated to have true anticachectic activity, so future research should be addressed to the identification of drugs able to block the activity of tumor-produced catabolic factors. The decision regarding optimum management of bowel obstruction should be individualized. Krebs' and Goplerud's score (based on age, nutritional status, tumor status, ascites, previous chemotherapy and irradiation) seems to offer reliable eligibility criteria for those patients who can benefit from surgery.

CT Check Tags: Female

Adrenergic beta-Antagonists: PD, pharmacology
Anaerobiosis
Animals
Anorexia: ET, etiology
Ascites: ME, metabolism
CHO Cells
*Cachexia: ET, etiology
Cachexia: PP, physiopathology
Cachexia: TH, therapy
Carbohydrate Metabolism
Cricetinae
Cricetulus
Cyclooxygenase Inhibitors: TU, therapeutic use
Cytokines: PH, physiology
Eicosapentaenoic Acid: TU, therapeutic use
Energy Metabolism: DE, drug effects
Fatty Acids: ME, metabolism
Floxuridine: TU, therapeutic use
Glycolysis
Humans
Interleukin-6: GE, genetics
Interleukin-6: PH, physiology
Intestinal Obstruction: ET, etiology
Intestinal Obstruction: SU, surgery
Intestinal Obstruction: TH, therapy
Intubation, Gastrointestinal
Linoleic Acid: ME, metabolism
Lipolysis: DE, drug effects
Lipoprotein Lipase: AI, antagonists & inhibitors
Megestrol Acetate: PD, pharmacology
Mice
Mice, Nude
Nausea: ET, etiology
*Nutrition Disorders: ET, etiology
Nutrition Disorders: PP, physiopathology
Nutrition Disorders: TH, therapy
*Ovarian Neoplasms: CO, complications
Ovarian Neoplasms: ME, metabolism
Palliative Care
Parenteral Nutrition, Total: AE, adverse effects
Proteins: ME, metabolism

Quality of Life
Transfection
Tumor Necrosis Factor-alpha: GE, genetics
Tumor Necrosis Factor-alpha: PH, physiology
RN **1553-41-9 (Eicosapentaenoic Acid)**; 2197-37-7 (Linoleic Acid); 3094-09-5 (doxifluridine); 50-91-9 (Floxuridine); 51154-23-5 (Megestrol Acetate)
CN 0 (Adrenergic beta-Antagonists); 0 (Cyclooxygenase Inhibitors); 0 (Cytokines); 0 (Fatty Acids); 0 (Interleukin-6); 0 (Proteins); 0 (Tumor Necrosis Factor-alpha); EC 3.1.1.34 (Lipoprotein Lipase)

L68 ANSWER 7 OF 12 MEDLINE on STN
AN 2001537493 MEDLINE
DN PubMed ID: 11346935
TI Current management of cancer-associated **anorexia** and weight loss.
AU Jatoi A Jr; Loprinzi C L
CS Division of Medical Oncology Mayo Clinic, Rochester, Minnesota, USA. Comprehensive Cancer Center, Northwestern University, Chicago, Illinois, USA.. w-small@northwestern.edu
SO Oncology (Williston Park, N.Y.), **(2001 Apr)** Vol. 15, No. 4, pp. 497-502, 508; discussion 508-10. Ref: 44
Journal code: 8712059. ISSN: 0890-9091.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 8 Oct 2001
Last Updated on STN: 8 Oct 2001
Entered Medline: 4 Oct 2001
AB Loss of appetite and weight predict a poor prognosis for cancer patients. Although caloric supplementation might benefit subgroups of patients--specifically, perioperative, severely malnourished cancer patients, stem cell and bone marrow transplant patients and head and neck cancer patients--its use remains controversial and is not recommended for the majority of patients with cancer-associated weight loss. Most patients with advanced cancer, **anorexia**, and/or weight loss do not appear to benefit from nutritional supplementation. Instead, discussions with patients and families about realistic eating goals ans, at time armacologic interventions with progestational agents or corticosteroids--both of which are aimed at palliating **anorexia** --provide clinical benefit. Other phamalogic interventions such as **eicosapentaenoic acid**, thalidomide (Thalomid), adenosine triphosphate and nonsteriodal anti-inflammatory agents focus on the fact that cancer-asscіated weight loss is an enitty dintinct for simple starvation These interventions promise to replenish lean tissue but require further investigation before they can be recommndedas standard clinical practice.
CT Algorithms
Anorexia: ET, etiology
***Anorexia: TH, therapy**
Humans
*Neoplasms: CO, complications
Nutritional Support: MT, methods
*Weight Loss: DE, drug effects
Weight Loss: PH, physiology

L68 ANSWER 8 OF 12 MEDLINE on STN

AN 2001299849 MEDLINE
DN PubMed ID: 11054609
TI Metabolic abnormalities in cachexia and **anorexia**.
AU Tisdale M J
CS Pharmaceutical Sciences Research Institute, Aston University, Birmingham, UK.. m.j.tisdale@aston.ac.uk
SO Nutrition (Burbank, Los Angeles County, Calif.), **(2000 Oct)** Vol. 16, No. 10, pp. 1013-4. Ref: 34
Journal code: 8802712. ISSN: 0899-9007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 4 Jun 2001
Last Updated on STN: 4 Jun 2001
Entered Medline: 31 May 2001
AB An increased glucose requirement by many solid tumors produces an increased metabolic demand on the liver, resulting in an increased energy expenditure. In addition, several cytokines and tumor catabolic products have been suggested as being responsible for the depletion of adipose tissue and skeletal-muscle mass in cachexia. A sulphated glycoprotein of molecular mass 24 kDa, produced by cachexia-inducing tumors and present in the urine of cancer patients actively losing weight, has been shown to be capable of inducing direct muscle catabolism in vitro and a state of cachexia in vivo, with specific loss of the non-fat carcass mass. In vitro studies have shown the bioactivity of this proteolysis-inducing factor to be attenuated by the polyunsaturated fatty acid, **eicosapentaenoic acid**. Preliminary clinical studies have shown that **eicosapentaenoic acid** stabilizes body weight and protein and fat reserves in patients with pancreatic carcinoma. Further trials are required to confirm the efficacy of **eicosapentaenoic acid** and to determine the anticachectic activity in other types of cancer.
CT ***Anorexia**: **ME**, **metabolism**
*Cachexia: ME, metabolism
*Carbohydrate Metabolism
Eicosanoic Acids: TU, therapeutic use
Humans
*Lipid Metabolism
*Proteins: ME, metabolism
CN 0 (Eicosanoic Acids); 0 (Proteins)

L68 ANSWER 9 OF 12 MEDLINE on STN
AN 1999115860 MEDLINE
DN PubMed ID: 9915907
TI Wasting in cancer.
AU Tisdale M J
CS Pharmaceutical Sciences Institute, Aston University, Birmingham B4 7ET, United Kingdom.
SO The Journal of nutrition, **(1999 Jan)** Vol. 129, No. 1S Suppl, pp. 243S-246S. Ref: 46
Journal code: 0404243. ISSN: 0022-3166.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals; AIDS
EM 199902

ED Entered STN: 11 Mar 1999
Last Updated on STN: 11 Mar 1999
Entered Medline: 22 Feb 1999

AB Progressive weight loss is a common feature of many types of cancer and is responsible not only for a poor quality of life and poor response to chemotherapy, but also a shorter survival time than is found in patients with comparable tumors without weight loss. Although **anorexia** is common, a decreased food intake alone is unable to account for the changes in body composition seen in cancer patients, and increasing nutrient intake is unable to reverse the wasting syndrome. Although energy expenditure is increased in some patients, cachexia can occur even with a normal energy expenditure. Various factors have been investigated as mediators of tissue wasting in cachexia. These include cytokines such as tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6), interferon-gamma (IFN-gamma) and leukemia inhibitory factor (LIF), as well as tumor-derived factors such as lipid mobilizing factor (LMF) and protein mobilizing factor (PMF), which can directly mobilize fatty acids and amino acids from adipose tissue and skeletal muscle respectively. Induction of lipolysis by the cytokines is thought to result from an inhibition of lipoprotein lipase (LPL), although clinical studies provide no evidence for an inhibition of LPL in the adipose tissue of cancer patients. Instead there is an increased expression of hormone sensitive lipase, the enzyme activated by LMF. Protein degradation in cachexia is associated with an increased activity of the ATP-ubiquitin-proteasome pathway. The biological activity of both the LMF and PMF was shown to be attenuated by **eicosapentaenoic acid** (EPA). Clinical studies show that this polyunsaturated fatty acid is able to stabilize the rate of weight loss and adipose tissue and muscle mass in cachectic patients with unresectable pancreatic cancer. Knowledge of the mechanism of cancer cachexia should lead to the development of new therapeutic agents.

CT **Anorexia: ME, metabolism**
Energy Metabolism: PH, physiology
*HIV Wasting Syndrome: ME, metabolism
HIV Wasting Syndrome: PA, pathology
Humans
Lipid Metabolism
Muscles: ME, metabolism
Weight Loss: PH, physiology

L68 ANSWER 10 OF 12 MEDLINE on STN
AN 1998052510 MEDLINE
DN PubMed ID: 9392617
TI Biology of cachexia.
AU Tisdale M J
SO Journal of the National Cancer Institute, **(1997 Dec 3)** Vol. 89, No. 23, pp. 1763-73. Ref: 138
Journal code: 7503089. ISSN: 0027-8874.
CM Comment in: J Natl Cancer Inst. 1998 Apr 15;90(8):628. PubMed ID: 9554447
Comment in: J Natl Cancer Inst. 1999 Jun 16;91(12):1077; author reply 1077-8. PubMed ID: 10379972
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 9 Jan 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 18 Dec 1997
AB About half of all cancer patients show a syndrome of cachexia,

characterized by loss of adipose tissue and skeletal muscle mass. Such patients have a decreased survival time, compared with the survival time among patients without weight loss, and loss of total body protein leads to substantial impairment of respiratory muscle function. These changes cannot be fully explained by the accompanying **anorexia**, and nutritional supplementation alone is unable to reverse the wasting process. Despite a falling caloric intake, patients with cachexia frequently show an elevated resting energy expenditure as a result of increases in Cori cycle (i.e., catalytic conversion of lactic acid to glucose) activity, glucose and triglyceride-fatty acid cycling, and gluconeogenesis. A number of cytokines, including tumor necrosis factor-apha, interleukins 1 and 6, interferon gamma, and leukemia-inhibitory factor, have been proposed as mediators of the cachectic process. However, the results of a number of clinical and laboratory studies suggest that the action of the cytokines alone is unable to explain the complex mechanism of wasting in cancer cachexia. In addition, cachexia has been observed in some xenograft models even without a cytokine involvement, suggesting that other factors may be involved. These probably include catabolic factors, which act directly on skeletal muscle and adipose tissue and the presence of which has been associated with the clinical development of cachexia. A polyunsaturated fatty acid, **eicosapentaenoic acid**, attenuates the action of such catabolic factors and has been shown to stabilize the process of wasting and resting energy expenditure in patients with pancreatic cancer. Such a pharmacologic approach may provide new insights into the treatment of cachexia.

CT *Cachexia: ET, etiology
*Cachexia: ME, metabolism
Cachexia: TH, therapy
Carbohydrate Metabolism
Growth Inhibitors: ME, metabolism
Humans
Interferon Type II: ME, metabolism
*Interleukin-6
Interleukins: ME, metabolism
Lipid Metabolism
Lymphokines: ME, metabolism
*Neoplasms: CO, complications
*Neoplasms: ME, metabolism
Peptides: ME, metabolism
Proteins: ME, metabolism
Tumor Necrosis Factor-alpha: ME, metabolism

RN 82115-62-6 (Interferon Type II)

CN 0 (Growth Inhibitors); 0 (Interleukin-6); 0 (Interleukins); 0 (Lymphokines); 0 (Peptides); 0 (Proteins); 0 (Tumor Necrosis Factor-alpha); 0 (leukemia inhibitory factor); 0 (lipid mobilizing substance)

L68 ANSWER 11 OF 12 MEDLINE on STN
AN 97352489 MEDLINE
DN PubMed ID: 9208884
TI The cancer cachexia syndrome.
AU Puccio M; Nathanson L
CS Winthrop University Hospital, Mineola, NY, USA.
SO Seminars in oncology, **(1997 Jun)** Vol. 24, No. 3, pp. 277-87.
Ref: 60
Journal code: 0420432. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LA English
FS Priority Journals
EM 199707
ED Entered STN: 5 Aug 1997
Last Updated on STN: 5 Aug 1997
Entered Medline: 23 Jul 1997
AB The cancer cachexia syndrome is clinically characterized by **anorexia**, wasting, weight loss, weakness, fatigue, poor performance status, and impaired immune function, which are unresolved by forced caloric intake. Diminished nutritional intake, maladaptive metabolic processes, and increased metabolic expenditure all play roles in the development of this syndrome. Multiple mediators of both tumor and host cell origin are mechanistic in its etiology. Treatment is not entirely satisfactory and should be directed toward improvement in the quality of life of the patient and should often include nutritional counseling. It should take into consideration both disease and treatment related factors as well as the cachexia syndrome itself. Use of progestogens (megesterol acetate, medroxyprogesterone), corticosteroids (decadron, prednisone), metoclopramide, tetrahydrocannabinol (dronabinol), and possibly anabolic steroids (nandrolone decanoate, oxandrolone), melatonin, and **eicosapentaenoic acid**, may yield therapeutic benefit.
CT **Anorexia: ET, etiology**
Appetite Stimulants
Cachexia: DI, diagnosis
*Cachexia: ET, etiology
Cachexia: PP, physiopathology
Cachexia: TH, therapy
Humans
*Neoplasms: CO, complications
Nutritional Support
Syndrome
CN 0 (Appetite Stimulants)

L68 ANSWER 12 OF 12 MEDLINE on STN
AN 93257719 MEDLINE
DN PubMed ID: 8490191
TI Cancer cachexia.
AU Tisdale M J
CS Pharmaceutical Sciences Institute, Aston University, Birmingham, UK.
SO Anti-cancer drugs, **(1993 Apr)** Vol. 4, No. 2, pp. 115-25. Ref: 102
Journal code: 9100823. ISSN: 0959-4973.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 25 Jun 1993
Last Updated on STN: 25 Jun 1993
Entered Medline: 16 Jun 1993
AB Cachexia is a common problem in the clinical management of cancer patients, particularly those with solid tumors. Cachexia is most obviously manifested as weight loss with massive depletion of both adipose tissue and muscle mass, and death is probably due to loss of lean body tissue. Not only is the survival time shorter in patients with cachexia, but the frequency of response to chemotherapy is also significantly reduced. Although **anorexia** frequently accompanies cachexia, attempts to halt or reverse cachexia by nutritional repletion have not

been successful. This suggests that cachexia is due to metabolic abnormalities produced by the tumor in addition to the underlying **anorexia**. In some patients weight loss is associated with an increased relative energy expenditure possibly through an elevated adrenergic state. Several factors have been postulated as mediators of cancer cachexia and can be divided into two groups. (i) Materials with hormone-like characteristics which result in direct catabolism of host tissues. (ii) Cytokines which cause alterations in host metabolism indirectly. Included in group (i) are the conventional catabolic hormones and a lipid mobilizing factor (LMF) produced by tumors, which causes direct breakdown of adipose tissue. Included in group (ii) are tumor necrosis factor-alpha, interleukin-6, interferon-gamma and leukaemia inhibitory factor. The materials appear to influence adipose tissue indirectly through an inhibition of lipoprotein lipase. Reversal of cachexia has been achieved by two groups of agents. (i) Those stimulating food intake, e.g. megestrol acetate. (ii) Those directly inhibiting the LMF, e.g. **eicosapentaenoic acid**. While agents in group (i) can cause tumor growth stimulation, those in group (ii) act as tumor growth inhibitors. This latter results suggests that the products of catabolism of host tissues may be important for tumor growth and provides a new avenue for chemotherapeutic intervention.

CT Animals
*Cachexia: ET, etiology
Cachexia: PP, physiopathology
Cachexia: TH, therapy
Humans
*Neoplasms: CO, complications
Research Support, Non-U.S. Gov't

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DNC C2005-151360

TI Composition, useful for controlling body weight, comprises (all-Z omega-3)-5,8,11,14,17-**eicosapentaenoic acid** and (all-Z omega-3)-4,7,10,13,16,19-docosahexaenoic acid.
DC B05 D13
IN BRYHN, M; KOPECKY, J
PA (PRON-N) PRONOVA BIOCARE AS
CYC 108
PI WO 2005060954 A1 20050707 (200550)* EN 61 A61K031-202
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT WO 2005060954 A1 WO 2004-IB4178 20041217
PRAI US 2003-530644P 20031219; SE 2003-3513 20031219
IC ICM A61K031-202
ICS A23L001-307; A61K031-557; **A61P003-04**
AB WO2005060954 A UPAB: 20050805
NOVELTY - In the production of a medicinal product for controlling body weight, for preventing body weight gain and for treatment and/or prevention of obesity or an overweight condition, a fatty acid composition comprising at least one of (all-Z omega-3)-5,8,11,14,17-**eicosapentaenoic acid** (EPA) and/or (all-Z omega-3)-4,7,10,13,16,19-docosahexaenoic acid (DHA) or their derivatives is used.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a dietary product containing the fatty acid composition, for non-medical treatment and/or prevention of obesity, an overweight condition and/or for supporting and controlling body weight reduction and/or for prevention of body weight gain.

ACTIVITY - Anorectic.

The effects of an omega-3 fatty acid composition containing EPA and DHA on the body weight were studied. A mixture containing EPA (approx. 20%) and DHA (50%) was used. Groups (n=7) of adult male mice (C57BL/6J mouse) fed standard feeding diet (4% fat), were randomly assigned one of four different types of semisynthetic high-fat (20% fat) diets where the fat component was: Group (I) Lard (L), Group (II) Lard plus EPAX2050TG (L+FO: EPAX 2050TG formed 44 weight/weight% of total lipid content), Group (III) Flaxseed oil (Ln) (18:3n-3 forms 50% of total lipids, Ln) and Group (IV) Flaxseed plus EPAX2050TG (Ln+FO; EPAX2050TG) (where FO is various EPA and DHA concentrates (for instance EPAX high in DHA versus EPAX high in EPA) used in these studies). The animals were fed the different diets during 1 month. After the study, the total body weight was reduced in Group (II) (L+FO) versus Group (I) (L); and Group (IV) (Ln+FO) versus Group (III) (Ln), and the difference was statistically significant in Group (IV) versus (III). The body weights of mice before treatment were similar in all the groups. The mice's given flaxseed oil plus EPAX2050TG had decreased by 10% in body weight compared to the mice's only given flaxseed oil. The study demonstrated that treatment with a fatty acid composition containing EPA and DHA leads to weight reduction.

MECHANISM OF ACTION - None given.

USE - The composition is useful for controlling body weight reduction, for preventing body weight gain and for treatment and/or prevention of obesity or an overweight condition. It is also useful for the production of a food stuff or food supplement in form of a flavored gelatine capsule for controlling and supporting body weight reduction

and/or for prevention of body weight gain; and as a dietary product (e.g. weight-watching product or slimming product). Also for supplementing a dietary product (all claimed).

ADVANTAGE - The composition reduces intake of calories in a human or animal. The composition has stronger body weight lowering effect.

Dwg.0/6

FS CPI

FA AB; DCN

MC CPI: B10-C04E; **B14-E12**; D03-H01G; D03-H01T2; D03-H01T3

TECH UPTX: 20050805

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: At lest one of EPA and DHA is obtained from at least one of vegetable, microbial and/or animal origin. At least a part of the EPA and/or DHA is produced from marine oil (preferably fish oil).

TECHNOLOGY FOCUS - FOOD - Preferred Composition: When the fatty acid composition is a liquid or an emulsion, then it is in a form of food stuff or food supplement is administrated as a beverage. The main active ingredient is DHA. The intake of the composition in the form of dietary product is combined with a reduced intake of calories for a human and/or together with physical activity. The dietary product is a bar, snack or beverage. The fatty acid composition is in liquid form or as an emulsion, for incorporation in a supplement product.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The weight ratio of EPA:DHA in the fatty acid composition is 1:greater than or equal to1 (preferably 1:1 - 1:8, 1:1 - 1:6). In the composition, the fatty acid is provided in at least one of esterified form, ethyl ester form, salt form and/or free acid form. The fatty acid composition is comprised of a combination of EPA and DHA in triglyceride form.

ABEX UPTX: 20050805

ADMINISTRATION - The daily dosage of the fatty acid composition is 1 - 15 (preferably 2 - 6) g for a human, and is administered in a daily dosage that corresponds to at least 10 (preferably 10 - 40)% of the total lipid content of a daily diet for a human or animal. The fatty acid composition is administered orally to human or animal (all claimed). The fatty acid composition may also be administered intravenously, subcutaneously, intramuscularly, intranasally, rectally, vaginally or topically.

M2 *01* DCN: **R04470-M; R04470-U; R04470-K; R13712-M; R13712-U; R13712-K**

M2 *02* DCN: R04471-M; R04471-U; R04471-K; R13713-M; R13713-U; R13713-K

L90 ANSWER 2 OF 3 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN **2004-269885** [25] WPIX

DNC C2004-105011

TI Use of **eicosapentaenoic acid** in the manufacture of a medicament for the treatment of **anorexia nervosa**, **bulimia** and related clinical syndromes.

DC B05

IN AYTON, A; HORROBIN, D F; DAVID, F H

PA (LAXD-N) LAXDALE LTD; (AMAR-N) AMARIN NEUROSCIENCE LTD

CYC 108

PI WO 2004024136 A1 20040325 (200425)* EN 31 A61K031-202

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003269138 A1 20040430 (200462) A61K031-202

NO 2005001847 A 20050415 (200534) A61K031-202
EP 1556028 A1 20050727 (200549) EN A61K031-202
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
ZA 2005002161 A 20051026 (200577) 34 A61K000-00
TW 2004010682 A 20040701 (200580) A61K031-202
JP 2006503031 W 20060126 (200609) 19 A61K031-185
CN 1694694 A 20051109 (200618) A61K031-202
BR 2003017857 A 20051206 (200624) A61K031-202

ADT WO 2004024136 A1 WO 2003-GB3985 20030916; AU 2003269138 A1 AU 2003-269138 20030916; NO 2005001847 A WO 2003-GB3985 20030916, NO 2005-1847 20050415; EP 1556028 A1 EP 2003-750919 20030916, WO 2003-GB3985 20030916; ZA 2005002161 A ZA 2005-2161 20050315; TW 2004010682 A TW 2003-125483 20030916; JP 2006503031 W WO 2003-GB3985 20030916, JP 2004-535695 20030916; CN 1694694 A CN 2003-825169 20030916; BR 2003017857 A BR 2003-17857 20030916, WO 2003-GB3985 20030916

FDT AU 2003269138 A1 Based on WO 2004024136; EP 1556028 A1 Based on WO 2004024136; JP 2006503031 W Based on WO 2004024136; BR 2003017857 A Based on WO 2004024136

PRAI GB 2002-21480 20020916

IC ICM A61K000-00; A61K031-185; A61K031-202
ICS A61K031-201; A61K031-21; A61K031-231; A61K031-232; A61P003-00; **A61P003-04**; A61P025-00

AB WO2004024136 A UPAB: 20040418
NOVELTY - In the manufacture of a medicament for the treatment of **anorexia nervosa**, **bulimia** and related clinical syndromes, **eicosapentaenoic acid** (EPA) is used.
ACTIVITY - Anabolic; Eating-Disorder-Gen.; Antiemetic.
A 15-year-old patient having 7.4-month history of dieting and eating difficulties had started with dietary restrictions and excessive exercise and proceeded to laxative abuse. Two months prior to being first seen she had stopped taking all solid food. She had lost 8 kg since stopping solid food, stopped menstruation and began to grow fine, downy lanugo hair over her body (common in **anorexia nervosa** (AN)). She was treated with a standard AN regime. This was ineffective and over the next two months she lost around 7 kg, which necessitated her admission to hospital. At this point she was extremely distressed and unable or unwilling to maintain a conversation. Her heart rate was very slow and her blood glucose was low, both signs of starvation. Over the following ten days she lost a further 5 kg in weight, to 42 kg. Her doctors believed that her life was in danger. She was treated with ethyl-**eicosapentaenoate** (E-EPA) (1 g/day). This transformed her response to treatment. Over the following weeks she began to eat normally and within 12 weeks she was back to 57 kg. Her mood and cognitive functions improved and she became normally communicative. Instead of being obsessed by weight and food to the exclusion of everything else, she became interested in all aspects of her life and her future. Her weight was 63/55/45/57/63 at pre-illness/1st doctor visit/hospitalization/dosing with E-EPA/3 moths after discharge.
MECHANISM OF ACTION - None given.
USE - In the manufacture of a medicament for the treatment of **anorexia nervosa**, **bulimia** and related clinical syndromes (claimed) e.g. vomiting disorders.
ADVANTAGE - The **eicosapentaenoic acid** provides an effective treatment for **anorexia nervosa**.
Dwg.0/5

FS CPI
FA AB; DCN
MC CPI: B05-B01P; B10-C04E; B10-D03; B10-E04C; B10-E04D; B10-G02; B14-E05; **B14-E11**

TECH UPTX: 20040418
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Drug: The EPA is taken from natural EPA-containing oil; in the form of the free acid, salt, mono-, di- or tri-glycerides, phospholipid, amide, ester or any other biologically compatible derivative (preferably triglycerides or ethyl ester, especially ethyl ester); is 70, preferably 95% pure; and contains less than 10 (preferably 5)% in aggregate and less than 3 (preferably 2)% individually of docosahexaenoic acid, linoleic acid or arachidonic acid.
ABEX UPTX: 20040418
ADMINISTRATION - EPA is administered in a dosage of 50 mg - 20 g/day (preferably 300 mg - 3 g/day) orally by adding to a nutritional supplement. EPA is also administered parenterally, intramuscularly, intravenously or by enteral tube (all claimed).
M1 *04* DCN: RA01PM-K; RA01PM-T; RA01PM-U
M2 *01* DCN: **R04470-K; R04470-T; R04470-U; R13712-K; R13712-T; R13712-U**
M2 *02* DCN: **R15961-K; R15961-T; R15961-U**
M2 *03* DCN: 0127-37401-K; 0127-37401-T; 0127-37401-U

L90 ANSWER 3 OF 3 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN **1997-011834** [01] WPIX
CR 2001-183074 [18]; 2001-191564 [19]; 2002-025885 [03]; 2002-443183 [47]; 2002-690385 [74]; 2004-675631 [66]
DNC C1997-003218
TI Compsn. to slow gastrointestinal transit of nutrients and bio-active(s) - to improve absorption, using active lipid, useful in treating diarrhoea, dumping syndrome, **anorexia**, post-surgery, etc..
DC B05
IN LIN, H C
PA (CEDA-N) CEDARS SINAI MEDICAL CENT
CYC 71
PI WO 9636330 A2 19961121 (199701)* EN 57 A61K031-20
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9658629 A 19961129 (199712) A61K031-20
EP 827402 A2 19980311 (199814) EN A61K031-20
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9608795 A 19990217 (199914) A61K031-20
JP 11505258 W 19990518 (199930) 60 A61K047-14
US 5977175 A 19991102 (199953) A61K031-20
MX 9708858 A1 19980801 (200014) A61K031-20
KR 99014865 A 19990225 (200018) A61K031-20
AU 722133 B 20000720 (200040) A61K031-20
MX 205865 B 20020107 (200307) A61K031-20
ADT WO 9636330 A2 WO 1996-US7165 19960516; AU 9658629 A AU 1996-58629 19960516; EP 827402 A2 EP 1996-920275 19960516, WO 1996-US7165 19960516; BR 9608795 A BR 1996-8795 19960516, WO 1996-US7165 19960516; JP 11505258 W JP 1996-535091 19960516, WO 1996-US7165 19960516; US 5977175 A Cont of US 1995-442843 19950517, US 1997-832307 19970403; MX 9708858 A1 MX 1997-8858 19971117; KR 99014865 A WO 1996-US7165 19960516, KR 1997-708210 19971117; AU 722133 B AU 1996-58629 19960516; MX 205865 B MX 1997-8858 19971117
FDT AU 9658629 A Based on WO 9636330; EP 827402 A2 Based on WO 9636330; BR 9608795 A Based on WO 9636330; JP 11505258 W Based on WO 9636330; KR 99014865 A Based on WO 9636330; AU 722133 B Previous Publ. AU 9658629, Based on WO 9636330
PRAI US 1995-442843 19950517; US 1997-832307 19970403
IC ICM A61K031-20; A61K047-14

AB WO 9636330 A UPAB: 20050218
Method for prolonging residence time of a substance in the small intestine, to allow absorption to occur, by admin. of an active lipid, is new.
USE - The method is used for enhancing the digestion and absorption of nutrients, and enhancing the absorption and bioavailability of pharmacologically active agents. Maximisation of nutrient and vitamin absorption is important after gastric, pancreatic, and/or intestinal surgery, in malnutrition, or in a range of disorders, including dumping syndrome, diarrhoea from a number of causes, steatorrhoea, asthenia, inflammatory bowel disease, peptide or endocrine tumours, cirrhosis, chronic alcohol dependence **anorexia**, bulaemia, endocrinopathies, and other enteropathies.
Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: B04-B01B; B10-C04E; **B14-E11**
M2 *01* DCN: 9701-33201-M; 9701-33201-U
M2 *02* DCN: R03769-M; R03769-U
M2 *03* DCN: R04038-M; R04038-U
M2 *04* DCN: R03770-M; R03770-U
M2 *05* DCN: R22533-M; R22533-U
M2 *06* DCN: R01226-M; R01226-U
M2 *07* DCN: R04471-M; R04471-U
M2 *08* DCN: **R04470-M; R04470-U**
M2 *09* DCN: R22531-M; R22531-U
M2 *10* DCN: R18178-M; R18178-U
M2 *11* DCN: R07145-M; R07145-U
M2 *12* DCN: R01147-M; R01147-U
M2 *13* DCN: R00206-M; R00206-U
M2 *14* DCN: R01269-M; R01269-U
M2 *15* DCN: R01356-M; R01356-U
M2 *16* DCN: R21538-M; R21538-U
M2 *17* DCN: R00954-M; R00954-U
M2 *18* DCN: R00121-M; R00121-U
M2 *19* DCN: R04540-M; R04540-U
M2 *20* DCN: R00122-M; R00122-U
M2 *21* DCN: R00758-M

```
=> e r04470+all/dcn
E1          647   -->  R04470/DCN
E2                 UF   EICOSAPENTAENOIC ACID, 5,8,11,14,17-/DCN
********** END **********

=> e r13712+all/dcn
E1          429   -->  R13712/DCN
E2                 UF   5,8,11,14,17-EICOSAPENTAENOIC ACID-SALTS(GEN)/DCN
********** END **********

=> e r15961+all/dcn
E1           50   -->  R15961/DCN
E2                 UF   EICOSAPENTAENOIC ETHYL ESTER/DCN
********** END **********

=> d his

     (FILE 'HOME' ENTERED AT 10:51:31 ON 10 MAY 2006)
               SET COST OFF
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     FILE 'HCAPLUS' ENTERED AT 10:51:37 ON 10 MAY 2006
                E HORROBIN/AU
L1           586 S E5,E8,E12-E16
                E AYTON/AU
L2             2 S E4
                E CLARKSON S/AU
L3            29 S E3-E6,E13
L4          8204 S EICOSAPENTAENOIC ACID OR EICOSAPENTAENOATE

     FILE 'REGISTRY' ENTERED AT 10:53:31 ON 10 MAY 2006
L5             1 S 10417-94-4
                E C20H30O2/MF
L6            17 S E3 AND 5 8 11 14 17
L7             8 S L6 AND EICOSAPENTAENOIC ACID
L8             6 S L7 NOT LABELED
                SEL RN
L9           160 S E1-E6/CRN
L10            6 S L5,L8

     FILE 'HCAPLUS' ENTERED AT 10:56:25 ON 10 MAY 2006
L11         9679 S L10
L12          652 S ICOSAPENT OR ICOSAPENTAENOIC ACID OR ICOSAPENTAENOATE OR TIMN
L13        12866 S L4,L11,L12
L14          100 S L9
L15          145 S L1-L3 AND L13
L16           12 S L1-L3 AND L14
L17          146 S L15,L16
                E ANOREXIA/CT
                E E3+ALL
L18         2355 S E2,E3
L19         7622 S ANOREX? OR ANOREX?(S)NERVOSA?
                E BULIMIA/CT
                E E3_ALL
                E BULIMIA/CT
                E E3+ALL
L20          932 S E1,E2
L21         1171 S BULIMI?
                E EATING DISORDER/CT
                E E4+ALL
L22         1983 S E2
L23         1432 S E1
L24            4 S L1-L3 AND L18-L23
L25            1 S L24 AND L17
L26            3 S L24 NOT L25
L27            1 S L26 AND 141:105641/DN
L28            2 S L25,L27
L29           54 S L17 AND P/DT
                E BODY WEIGHT/CT
L30        22053 S E3-E5
                E E3+ALL
L31        64675 S E2 OR E5+OLD,NT OR E6+OLD,NT OR E7+OLD,NT OR E8+OLD,NT
L32          475 S L13 AND L30,L31
L33           22 S L32 AND L18-L23

     FILE 'REGISTRY' ENTERED AT 11:04:16 ON 10 MAY 2006
L34            1 S 25378-27-2
L35           17 S 25378-27-2/CRN

     FILE 'HCAPLUS' ENTERED AT 11:04:46 ON 10 MAY 2006
L36         1055 S L34 OR L35
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L37           2 S L36 AND L18-L23
L38          30 S L36 AND L30,L31
L39           2 S L37 AND L38
L40          22 S L33,L39
L41          11 S L1-L3 AND L36
L42           0 S L41 AND L39
L43           0 S L41 AND L40
                 SEL AN L40 4 7-9 12 16-21
L44          11 S L40 AND E1-E22
L45          13 S L28,L44
L46          13 S L45 AND L1-L4,L11-L33,L36-L45

     FILE 'REGISTRY' ENTERED AT 11:14:19 ON 10 MAY 2006
L47              STR
L48           36 S L47 CSS
L49          756 S L47 CSS FUL
                 SAV L49 JONES528/A
L50          590 S L49 NOT L9,L10

     FILE 'HCAPLUS' ENTERED AT 11:21:15 ON 10 MAY 2006
L51          712 S L50
L52            1 S L51 AND L18-L23
L53            7 S L51 AND L30,L31
L54            8 S L52,L53
L55            0 S L46 AND L51

     FILE 'REGISTRY' ENTERED AT 11:24:39 ON 10 MAY 2006

     FILE 'HCAPLUS' ENTERED AT 11:24:51 ON 10 MAY 2006

     FILE 'MEDLINE' ENTERED AT 11:26:18 ON 10 MAY 2006
L56         2311 S L9 OR L10 OR L50 OR L34 OR L35
L57         3876 S L4 OR L12
L58         3877 S L56,L57
L59        21444 S L19 OR L21
                 E ANOREXIA/CT
                 E E3+ALL
L60         2730 S E5+NT
                 E E8+ALL
L61         7839 S E4+NT
                 E E3+ALL
L62        14422 S E3+NT
                 E BULIMIA/CT
                 E E3+ALL
L63         4008 S E6+NT OR E11+NT
L64           22 S L58 AND L59-L63
L65            9 S L64 AND PY<=2002
L66           13 S L64 NOT L65
L67            3 S L66 AND 2003/PY
L68           12 S L65,L67

     FILE 'MEDLINE' ENTERED AT 11:30:07 ON 10 MAY 2006

     FILE 'WPIX' ENTERED AT 11:30:21 ON 10 MAY 2006
L69         1082 S L4 OR L12
L70           57 S EICOSA PENTAEN?
L71            0 S EICOSA PEN TAEN?
L72            2 S EICO SAPENTAEN?
                 E EICOSAPENTAEN/CN
L73            9 S E4-E20
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                SEL SDCN
                EDIT /SDCN /DCN
L74          686 S E1-E10
                SEL DCSE L73
                EDIT E11-E19 /DCSE /DCRE
L75          438 S E11-E19
L76         1355 S L69-L72,L74,L75
L77         4356 S L19 OR L21
L78         4321 S A61P003-04/IPC,IC,ICM,ICS,ICA,ICI
L79        27920 S (B12-J02 OR B14-E12 OR B14-E11? OR C12-J02 OR C14-E12 OR B14-
L80           13 S L76 AND L77
L81           19 S L76 AND L78
L82          168 S L76 AND L79
L83          170 S L80,L81,L82
L84          135 S L69 AND L83
L85            2 S L70,L72 AND L83
L86          135 S L84,L85
L87           35 S L83 NOT L86
                E R04470+ALL/DCN
                SEL AN 30
L88            1 S E1 AND L87
                SEL AN L86 15 46
L89            2 S L86 AND E2-E3
L90            3 S L88,L89 AND L69-L89

     FILE 'WPIX' ENTERED AT 11:49:37 ON 10 MAY 2006
                E R04470+ALL/DCN
                E R13712+ALL/DCN
                E R15961+ALL/DCN

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